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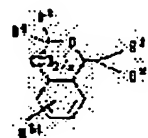
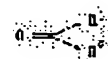
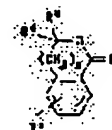
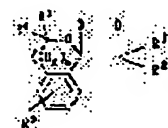
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(54) 1,2-DIOXETANE DERIVATIVE BONDED TO OXOBENZOCYCLOALKENE RING IN SPIRO STATE

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain a new 1,2-dioxetane derivative useful for the immunoassay or the like as a chemical luminescent reagent.

SOLUTION: A compound of formula I [R1-R4 are each H, an alkyl or an aryl; R1 and R2 or R3 and R4 are respectively combined to form a cyclic alkyl; R5 is hydroxyl, an alkoxy, an aralkyloxy, OSi(R6R7R8) (R6-R8 are each an alkyl) or a phosphoric base; (n) is 0-2], e.g. 6'-t-butyldimethylsiloxy-1',3'-dihydro-4,4'-diisopropyl-3',3'-dimethylspiro-[1,2-dioxetane-3,1'-isobenzofuran], the compound of formula I is obtained by reacting a compound of formula IV prepared by reacting a compound of formula II with a compound of formula III with singlet oxygen.



LEGAL STATUS

[Date of request for examination]

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decision of rejection]

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JAPANESE

[JP,09-157271,A]

CLAIMS DETAILED DESCRIPTION TECHNICAL FIELD PRIOR ART EFFECT OF THE INVENTION
TECHNICAL PROBLEM MEANS EXAMPLE

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*** NOTICES ***

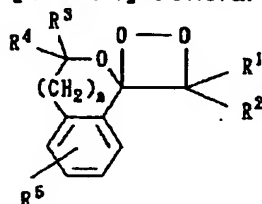
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CLAIMS

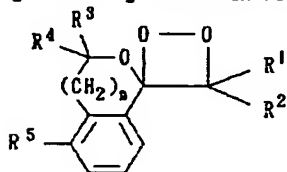
[Claim(s)]

[Claim 1] General formula. [Formula 1]



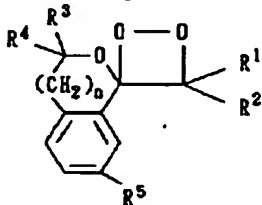
1 come out of and expressed, 2-JIOKI cetane derivative (R^1 , R^2 , R^3 , and R^4 are a hydrogen atom, an alkyl group, or an aryl group among a formula.) Moreover, R^1 , R^2 , R^3 , R^4 It is united and an annular alkyl group can also be formed. R^5 They are a hydroxyl, an alkoxyl group, an aralkyloxy machine, $-OSi$ (R^6 , R^7 , R^8) (however, R^6 , R^7 , and R^8 are alkyl groups independently mutually.), or a phosphate machine. n is 0, 1, or 2.

[Claim 2] General formula. [Formula 2]



1 according to claim 1 come out of and expressed, 2-JIOKI cetane derivative.

[Claim 3] General formula. [Formula 3]



1 according to claim 1 come out of and expressed, 2-JIOKI cetane derivative.

[Claim 4] R^1 , R^2 , and R^3 And R^4 1 according to claim 1 which is an alkyl group, 2-JIOKI cetane derivative.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[The technical field to which invention belongs] this invention relates to new 1 and 2-JIOKI cetane derivative. 1 of this invention and 2-JIOKI cetane derivative can be used for immunoassay etc. as a chemiluminescence reagent.

[0002]

[Description of the Prior Art] Conventionally, various 1 and 2-JIOKI cetane derivatives are compounded, and it is known that the compound which the SUPRO adamantyl machine combined especially with the 3rd place is useful as a chemiluminescence substrate (for example, refer to a JP,5-21918,B specification and a JP,5-45590,B specification).

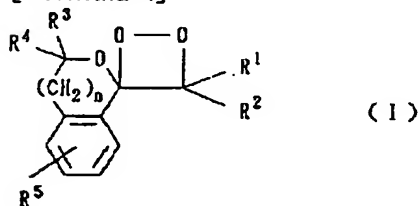
[0003]

[Problem(s) to be Solved by the Invention] However, it could not say that there was the conventional compound about sufficient effect to luminescence durability, but the improvement was desired.

[0004]

[Means for Solving the Problem] An invention-in-this-application person is a general formula (I), as a result of inquiring wholeheartedly that the fault which the conventional compound has should be conquered.

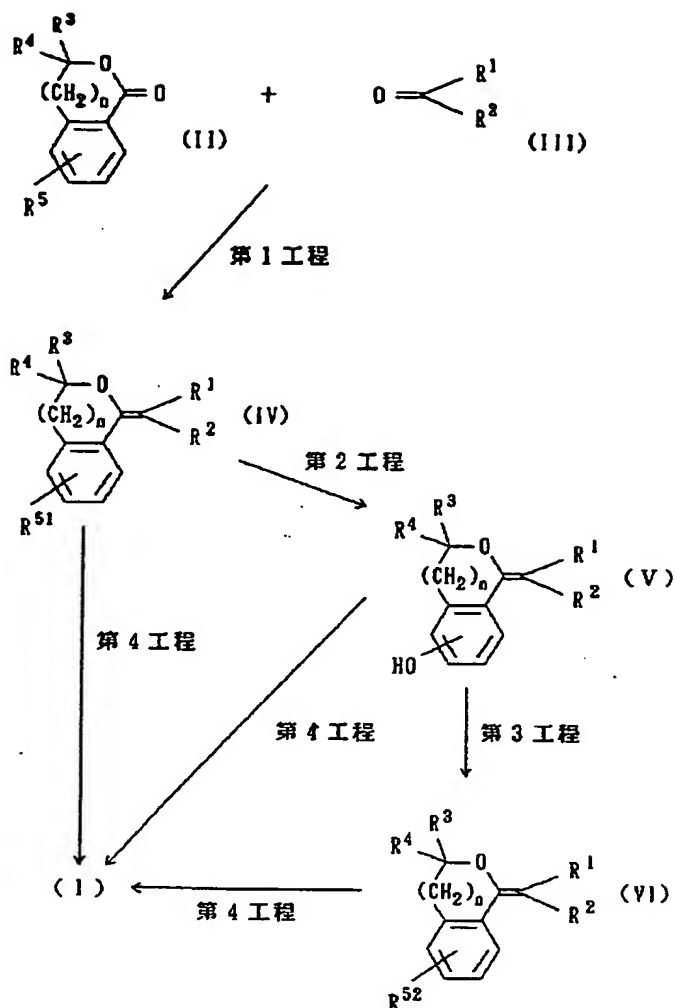
[Formula 4]



(R1, R2, R3, and R4 are a hydrogen atom, an alkyl group, or an aryl group among a formula.) Moreover, R1 R2 And R3 R4 It is united and an annular alkyl group can also be formed. R5 They are a hydroxyl, an alkoxy group, an aralkoxy machine, -OSi (R6 R7 R8) (however, R6, R7, and R8 are alkyl groups independently mutually.), or a phosphate machine. n is 0, 1, or 2. 1 expressed and 2-JIOKI cetane derivative are found out, and this invention is completed.

[0005] 1 expressed with the aforementioned general formula (I) of this invention and 2-JIOKI cetane derivative can be manufactured according to the following reaction formulae.

[Formula 5]



(R1 -R5 is the same as the above among a formula.) R51 is an alkoxyl group or an aralkyloxy machine, and R52 is -OSi (R6 R7 R8) (R6 -R8 is the same as the above.), or a phosphate machine.

[0006] In explaining this invention in detail hereafter by this invention with an "alkyl group" The alkyl group of the shape of the shape of a straight chain of 1-20 carbon numbers which may have the substituent, and a branched chain is said. the alkyl group A methyl, ethyl, a propyl, butyl, a pentyl, a hexyl, a heptyl, The basis which the basis and the aforementioned alkyl group of a straight chain of an octyl, a nonyl, a desyl, a undecyl, a dodecyl, tetradecyl, pentadecyl, hexadecyl one, heptadecyl, octadecyl, a nona desyl, and IKODESHIRU combined in the shape of branching suitably is said. The bases which may carry out [aforementioned] substitution are a hydroxyl, an alkoxyl group, an aryl group, a heterocycle machine, etc. As the alkoxyl group, it is methoxy and ethoxy ** propoxy, butoxy one, pentyloxy one, hexyloxy one, methoxyethoxy one, methoxy propoxy, ethoxy ethoxy ** ethoxy propoxy one, a methoxyethoxy ethoxy basis, etc., and as the aryl group, it is a phenyl, a naphthyl group, etc. and they are a furil, a thienyl, a pyridyl machine, etc. as the heterocycle machine, for example.

[0007] Moreover, it is the same as the alkoxyl group which may be replaced by the alkyl group described above as the "alkoxyl group" by this invention, and an "aryl group" points out an aromatic-hydrocarbon machine and the hetero aryl groups which have nitrogen, oxygen, or a sulfur atom endocyclic, such as a phenyl and a naphthyl group. Furthermore, "aralkyloxy machines" is a benzyloxy machine, a phenethyloxy machine, etc.

[0008] (The 1st process) This process is the 2 ring type lactone and the general formula (III) which are expressed with a general formula (II). The ketone expressed is made to react and the alkene derivative expressed with a general formula (IV) is manufactured.

[0009] It is desirable to make to perform a reaction to the bottom of existence of titanium into indispensable requirements, and to use halogenation titanium, such as a titanium chloride, as titanium.

[0010] Moreover, as a reducing agent, it is desirable to make reduced condition form using a triethylamine, a pyridine, etc. as bases, such as lithium-hydride aluminum, and to present a reaction.

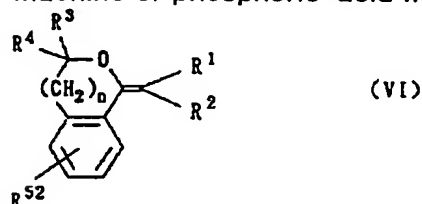
[0011] In reacting, it can carry out in the organic ether, such as a tetrahydrofuran (THF).

[0012] Although a reaction advances at 0-100 degrees C, it is desirable from operation and a reactant viewpoint to carry out to the bottom of reflux of THF

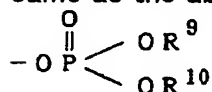
[0013] (The 2nd process) This process manufactures the alcoholic derivative which performs the deprotection reaction of a compound expressed with the aforementioned general formula (IV), and is expressed with a general formula (V).

[0014] As a compound with which a deprotection reaction is presented, it is the aforementioned general formula (IV) (R1 -R4 is the same as the above). R51 is the protective group (they are a methoxy machine and a benzyloxy machine preferably.) of a hydroxyl group. it is — although it can carry out whether a reaction is performed by making the anion of the method known well by this contractor, i.e., an alkyl thiol, react, and by giving a hydrogenation reaction, which reaction is chosen should just choose suitably by the basis which should be carried out a deprotection

[0015] (The 3rd process) The halogenation trialkyl silane or halogenation phosphate corresponding to the compound expressed with the aforementioned general formula (V) is made to react for silyloxy machine or phosphoric-acid machine formation, and this process is a general formula (VI). [Formula 6]



the inside of a formula, and R1 -R4 — the above — the same — R52 -OSi (R6 R7 R8) (R6 -R8 is the same as the above.) — or . [Formula 7]



It comes out. R9 And R10 is an alkyl group or R9, and the basis that R10 are united and may form a ring. The compound expressed is manufactured.

[0016] Furthermore, in this process, when chloroethylene phosphate is made to react for phosphoric-acid machine introduction, it changes into the sodium salt of cyano ethyl phosphate by the sodium cyanide, and is further desorbed from a cyano ethyl group, and it is ammonium. It is convertible for sodium salt. This ammonium Sodium salt is easily convertible for disodium salt by making it react with a sodium hydrogencarbonate.

[0017] (The 4th process) The alkene derivative expressed with a general formula (IV), (V), or (VI) is made to react with a singlet oxygen, and this process is the aforementioned general formula (I). 1 expressed and 2-JIOKI cetane derivative are manufactured.

[0018] The reaction with a singlet oxygen dissolves the alkene derivative expressed with the aforementioned general formula (IV), (V), or (VI) in solvents, such as alcohol, such as halogenated hydrocarbons, such as a dichloromethane, a dichloroethane, and a carbon tetrachloride, or a methanol, and ethanol, and is attained by performing light irradiation under oxygen atmosphere under coexistence of photosensitizers, such as a methylene blue, a rose bengal, and a tetraphenylporphine. In addition, a reaction is performed at -80 degrees C - a room temperature.

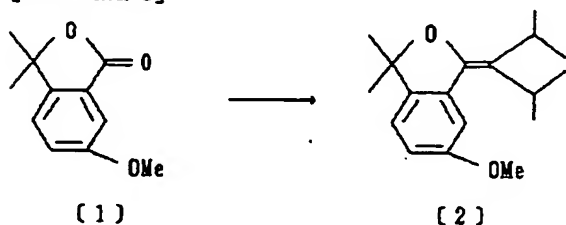
[0019] Hereafter, an example and the example of reference explain this invention in detail.

[0020]

[Example]

(Example 1 of reference)

[Formula 8]



anhydrous in the bottom of argon atmosphere, and 5.3g (34.4mmol) of titanium trichlorides — after suspending in THF100ml and stirring for 15 minutes, it ice-cooled, lithium-hydride aluminum 660mg (17.4mmol) was added, and it stirred for 30 minutes at the room temperature Triethylamine 2.4ml (17.2mmol) was added to this solution, and heating reflux was carried out for 30 minutes. anhydrous [in

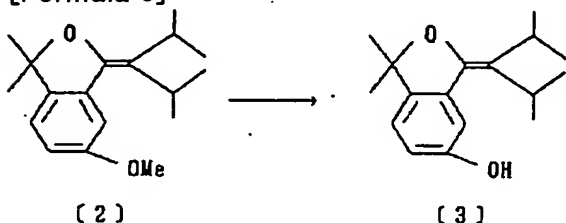
6-methoxy -1, 3-dihydro-3 and 3-dimethyl iso benzofuran-1-yl (compound [1]) 655mg (3.41mmol) and diisopropyl keton 1.0ml (7.06mmol)] in this solution — it dissolved in THF20ml, and it applied for 45 minutes, and was dropped, and heating reflux was carried out for further 1 hour Reaction mixture was invested in iced water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness one by one with water, sodium-hydrogencarbonate solution, and saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 20:1 of a hexane and ethyl acetate, it is 1-diisopropyl methylidyne. - 1, the 3-dihydro-6-methoxy -3, and the 3-dimethyl iso benzofuran (compound [2]) were obtained at 497mg and 53.6% of yield.

[0021] Melting point; 86.0 to 87.0 degree C (it recrystallizes from a colorless plate crystal and a methanol)

¹HNMR(300MHz and CDCl₃);delta 1.10 (d, J= 6.9Hz, 6H), 1.25(d,J=7.0Hz,6H),1.48(s,6H),2.45 (sept,J=7.0Hz,1H),3.33(sept,J=6.9Hz,1H),3.82(s,3H),6.79(dd,J=8.3 and 2.2Hz,1H),7.04(d,J=8.3Hz,1H) and 7.14(d,J=2.2Hz,1H)ppmIR(KBr);2960,2932,1648,1616 and 1584cm⁻¹Mass(m/z,%);274(M+ ,35),259(100) and231(24)

[0022] (Example 2 of reference)

[Formula 9]

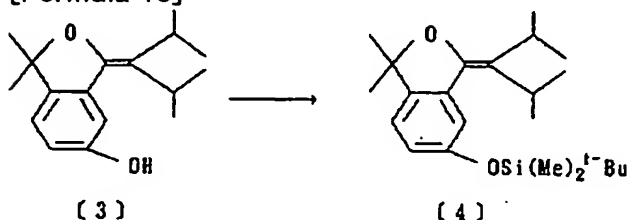


anhydrous in 80mg (2.00mmol) of 60% sodium hydrides — ethanethiol 0.15ml (2.03mmol) was added to the solution which suspended in DMF2ml and was stirred at 0 degree C under argon atmosphere, and it stirred for 20 minutes anhydrous in compound [2]150mg (0.547mmol) compounded in the example 1 of reference in this solution — it dissolved in DMF1ml and, in addition, heating reflux was carried out for 3 hours Reaction mixture was invested in saturation brine and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 5:1 of a hexane and ethyl acetate, it is 1-diisopropyl methylidyne. - 1, 3-dihydro-6-hydroxy - The 3 and 3-dimethyl iso benzofuran (compound [3]) was obtained as a colorless viscosity object at 135mg and 94.9% of yield.

[0023] ¹HNMR(400MHz and CDCl₃);delta 1.09 (d, J= 6.8Hz, 6H), 1.25(d,J=6.8Hz,6H),1.25(s,6H),2.44 (sept,J=6.8Hz,1H), 3.29(sept,J=6.8Hz,1H),4.81(broad s,1H), 6.70(dd,J=7.8and 2.4Hz,1H),6.98(d,J=7.8Hz,1H), 7.08(d,J=2.4Hz,1H)ppmIR(liq.film);3385,2970,1735,1610cm⁻¹Mass(m/z,%);260(M+ ,22),245(100),217(39),205 (63),163([37]

[0024] (Example 3 of reference)

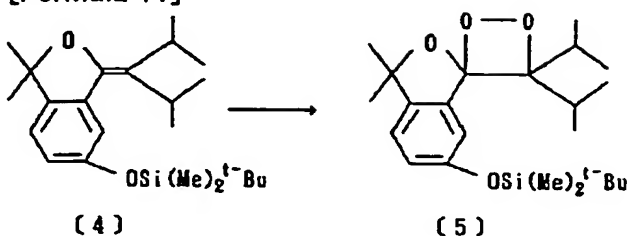
[Formula 10]



anhydrous in compound [3]130mg (0.500mmol) compounded in the example 2 of reference — it dissolved in DMF2ml and stirred at 0 degree C under argon atmosphere Triethylamine 1.0ml (7.17mmol) and t-butyldimethyl chlorosilane 0.10g (0.663mmol) were added to this solution, and it stirred at the room temperature for 1 hour. Reaction mixture was invested in water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 10:1 of a hexane and ethyl acetate, it is 6-t-butyldimethylsiloxy-1-diisopropyl methylidyne. - 1, 3-dihydro - The 3 and 3-dimethyl iso benzofuran (compound [4]) was obtained as colorless oily matter at 152mg and 81.3% of yield.

[0025] ¹HNMR(400MHz and CDCl₃);delta 0.21 (s, 6H), 0.99(s,9H),1.10(d,J=6.8Hz,6H),1.25 (d,J=6.8Hz,6H),1.47(s,6H),2.45(sept,J=6.8Hz,1H),3.28(sept,J=6.8Hz,1H),6.70(dd,J=7.8 and 2.0Hz,1H),6.95 (d,J=7.8Hz,1H),7.05(d,J=2.0Hz,1H)ppmIR(KBr);2955,1610,1285cm⁻¹Mass(m/z,%);374(M+ ,32),259(100),331 (15)

(13)
[0026] (Example 1)
[Formula 11]

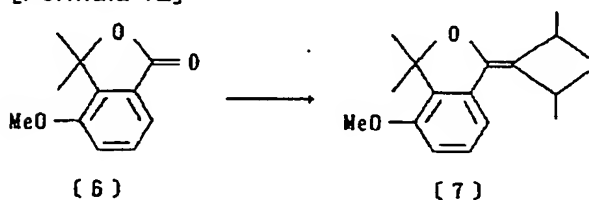


Compound [4] 100mg (0.267mmol) compounded in the example 3 of reference and TPP5mg were dissolved in dichloromethane 10ml, and it stirred at -78 degrees C under oxygen atmosphere. The sodium lamp (940W) performed optical irradiation in this solution for 2 hours. the place which condenses reaction mixture, and applies a concentrate to a silica gel column, and it began to pass by the mixed solvent of 10:1 of a hexane and ethyl acetate — 6 — 't-butyl dimethylsiloxy-1', 3'-dihydro-4, and 4-diisopropyl-3', 3' - dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' - iso benzofuran] (compound [5]) — 97mg and 89.4% of yield — as light yellow oily matter It was obtained.

[0027] ¹HNMR(400MHz and CDCl₃);delta 0.22 (s, 3H), 0.23(s,3H),0.74(d,J=7.3Hz,3H),0.99(d,J=7.3Hz,3H), 1.01(s,9H),1.18(d,J=7.3Hz,3H),1.35(d,J=7.3Hz,3H), 1.47(s,3H),1.55(s,3H),2.89(sept,J=7.3Hz,1H), 3.08 (sept,J=7.3Hz,1H),6.92(dd,J=8.3 and 2.4Hz,1H), 6.99(d,J=8.3Hz,1H),7.39(d,J=2.4Hz,1H)ppmIR(liq.film);29 65 and 2860, 1255cm⁻¹Mass(m/z, %);374 (32 M+ - 18), 235 (100) 259 (17), 292 (22), 217 (11)

[0028] (Example 4 of reference)

[Formula 12]



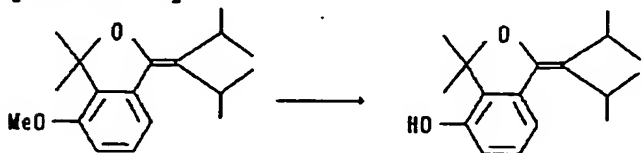
anhydrous in the bottom of argon atmosphere, and 5.0mg (32.4mmol) of titanium trichlorides — after suspending in THF100ml and stirring for 15 minutes, it ice-cooled, lithium-hydride aluminum 632mg (16.7mmol) was added, and it stirred for 30 minutes at the room temperature Triethylamine 2.3ml (16.5mmol) was added to this solution, and heating reflux was carried out for 30 minutes. anhydrous [in 1, 3-dihydro-4-methoxy -3 and 3-dimethyl iso benzofuran-1-ON (compound [6]) 625mg (3.26mmol) and diisopropyl keton 0.96ml (6.78mmol)] in this solution — it dissolved in THF20ml, and it applied for 10 minutes, and was dropped, and heating reflux was carried out for further 1 hour Reaction mixture was invested in iced water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness one by one with water, sodium-hydrogencarbonate solution, and saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 30:1 of a hexane and ethyl acetate, it is 1-diisopropyl methylidyne. - 1, the 3-dihydro-4-methoxy -3, and the 3-dimethyl iso benzofuran (compound [7]) were obtained at 544mg and 61.0% of yield.

[0029] Melting point; 48.0 to 48.5 degree C (it recrystallizes from colorless granular ** and a methanol) ¹HNMR(300MHz and CDCl₃);delta 1.09 (d, J= 6.8Hz, 6H), 1.25(d,J=7.0Hz,6H),1.56(s,6H),2.43 (sept,J=7.0Hz,1H),3.37(sept,J=6.8Hz,1H),3.84(s,3H),6.69-6.77(m,1H),7.18-7.26(m,2H)ppmIR

(KBr);2968,2868,1648,1606,1588cm⁻¹Mass(m/z,%);274(M+ ,68),260(44),259(100),231(58),217(13),189(17)

[0030] (Example 5 of reference)

[Formula 13]



[7]

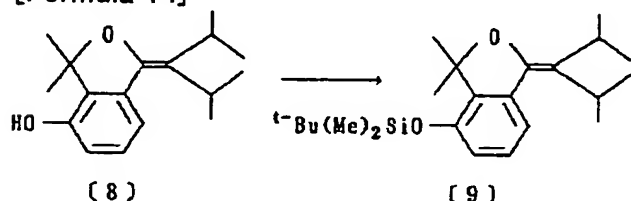
[8]

anhydrous in compound [7] 371mg (1.36mmol) compounded 60% in 126mg (3.15mmol) of sodium hydrides, and the example 4 of reference — it suspended in DMF 4.5ml, ethanethiol 0.22ml (2.97mmol) was added to the solution stirred at 0 degree C under argon atmosphere, and it stirred for 10 minutes. The heating reflux of this solution was carried out for 2 hours. Reaction mixture was invested in saturation brine and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of a hexane and ethyl acetate, it is 1-diisopropyl methylidyne-1,3-dihydro-4-hydroxy-3,3-dimethyl iso benzofuran (compound [8]) was obtained at 335mg and 95.2% of yield.

[0031] Melting point; 98.0 to 98.5 degree C (it recrystallizes from colorless granular ** and a hexane) ¹H NMR (300MHz and CDCl₃); δ 1.09 (d, J=6.8Hz, 6H), 1.26 (d, J=7.0Hz, 6H), 1.60 (s, 6H), 2.44 (sept, J=7.0Hz, 1H), 3.36 (sept, J=6.8Hz, 1H), 4.65 (s, 1H), 6.57 (d, J=7.8Hz, 1H), 7.11 (t, J=7.8Hz, 1H), 7.22 (d, J=7.8Hz, 1H) ppm IR (KBr); 3516, 2976, 1646, 1616, 1588 cm⁻¹ Mass (m/z, %); 260 (M⁺, 33), 245 (100), 217 (32)

[0032] (Example 6 of reference)

[Formula 14]



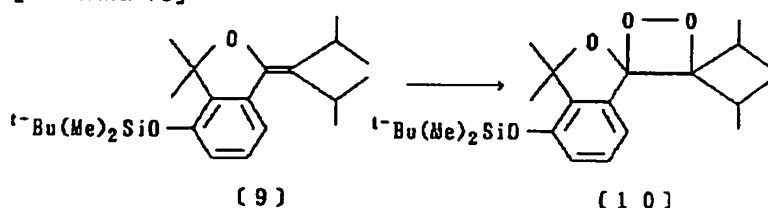
anhydrous in compound [8] 231mg (0.89mmol) compounded in the example 5 of reference — it dissolved in DMF 3ml and stirred at 0 degree C under argon atmosphere. Imidazole 130mg (1.91mmol) and t-butyldimethyl chlorosilane 220mg (1.46mmol) were added to this solution, and it stirred at the room temperature overnight. Reaction mixture was invested in water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the hexane, it is 4-t-butyldimethylsiloxy-1-diisopropyl methylidyne-1,3-dihydro-3,3-dimethyl iso benzofuran (compound [9]) was obtained at 274mg and 82.5% of yield.

[0033] Melting point; 83.5 to 84.0 degree C (it recrystallizes from a colorless needle shape crystal, a methanol, and ethyl acetate)

¹H NMR (300MHz and CDCl₃); δ 0.30 (s, 6H), 1.02 (s, 9H), 1.08 (d, J=6.8Hz, 6H), 1.25 (d, J=7.0Hz, 6H), 1.57 (s, 6H), 2.43 (sept, J=7.0Hz, 1H), 3.36 (sept, J=6.8Hz, 1H), 6.67 (d, J=7.9Hz, 1H), 7.11 (t, J=7.9Hz, 1H), 7.21 (d, J=7.9Hz, 1H) ppm IR (KBr); 2956, 1646, 1588, 1274 cm⁻¹ Mass (m/z, %); 374 (M⁺, 32), 360 (29), 359 (100), 331 (20)

[0034] (Example 2)

[Formula 15]

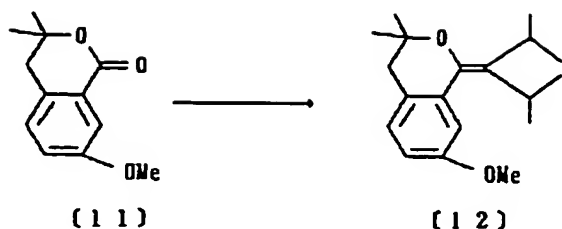


Compound [9] 60mg (0.16mmol) compounded in the example 6 of reference and TPP 3mg were dissolved in dichloromethane 20ml, and it stirred at -78 degrees C under oxygen atmosphere. The sodium lamp (180W) performed optical irradiation in this solution for 2 hours. The place which condenses reaction mixture, and applies a concentrate to a silica gel column, and it began to pass by the mixed solvent of 10:1 of a hexane and ethyl acetate — 4-t-butyldimethylsiloxy-1,3-dihydro-4,4-dimethyl-2H-pyran-2-one — 39mg and 59.9% of yield — as a colorless indeterminate form it was obtained.

[0035] ¹H NMR (300MHz and CDCl₃); δ 0.29 (s, 3H), 0.33 (s, 3H), 0.73 (d, J=7.4Hz, 3H), 0.98 (d, J=7.0Hz, 3H), 1.02 (s, 9H), 1.18 (d, J=7.1Hz, 3H), 1.35 (d, J=7.1Hz, 3H), 1.57 (s, 3H), 1.64 (s, 3H), 2.82-2.98 (m, 1H), 3.04-3.21 (m, 1H), 6.84 (d, J=8.0Hz, 1H), 7.26 (dd, J=8.0 and 7.8Hz, 1H), 7.56 (d, J=7.8Hz, 1H) ppm IR (KBr); 2968, 2940, 1602, 1288 cm⁻¹ Mass (m/z, %); 374 (32 M⁺ - 6), 359 (7), 292 (25), 236 (22), 235 (100)

[0036] (Example 7 of reference)

[Formula 16]

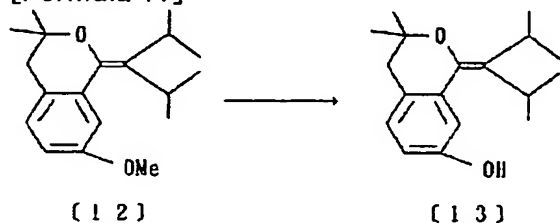


anhydrous [in 4.5g (29.2mmol) of titanium trichlorides] at the bottom of nitrogen atmosphere, and 0 degree C — lithium-hydride aluminum 570mg (15.0mmol) was added to the solution suspended in THF75ml, and it stirred at the room temperature Triethylamine 2.10ml (15.1 mmol) was added to this solution, and heating reflux was carried out for 15 minutes. anhydrous [in 7-methoxy -3 and 3-dimethyl iso chroman-1-ON (compound [11]) 380mg (1.84mmol) and diisopropyl keton 1.8ml (12.7mmol)] in this solution — it dissolved in THF25ml, and it applied for 20 minutes, and was dropped, and heating reflux was carried out for further 1 hour Reaction mixture was invested in iced water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with water. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 3:1 of a hexane and a dichloromethane, the 1-diisopropyl methylidyne-7-methoxy -3 and the 3-dimethyl iso chroman (compound [12]) were obtained as colorless oily matter at 215mg and 40.5% of yield.

[0037] ¹HNMR(400MHz and CDCl₃);delta1.04 (d, J= 6.8Hz, 6H), 1.15(s,6H),1.28(d,J=6.8Hz,6H),2.37 (sept,J=6.8Hz,1H),2.60(s,2H),3.12(sept,J=6.8Hz,1H),3.80(s,3H),6.75(dd,J=8.3 and 2.4Hz,1H),6.88 (d,J=2.4Hz,1H),7.00(t,J=8.3Hz,1H)ppmMass(m/z,%);288(M+ ,6),287(21),272(39),244(29),188(43),174(16),148 (100)

[0038] (Example 8 of reference)

[Formula 17]

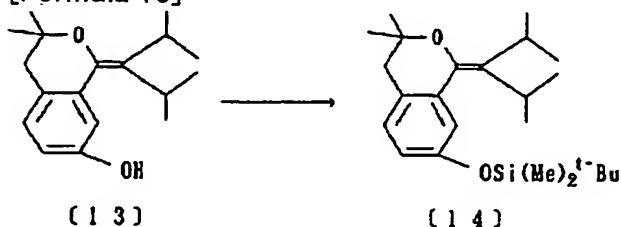


anhydrous in 80mg (2.00mmol) of 60% sodium hydrides — it suspended in DMF2ml, ethanethiol 0.15ml (2.03mmol) was added to the solution stirred at 0 degree C under argon atmosphere, and it stirred for 20 minutes anhydrous in compound [12] 175mg (0.608mmol) compounded in the example 7 of reference in this solution — it dissolved in DMF1ml and, in addition, heating reflux was carried out for 3 hours Reaction mixture was invested in saturation brine and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of a hexane and ethyl acetate 5:1, it is 1-diisopropyl methylidyne-7-hydroxy. - 3 and 3-dimethyl chroman (compound [13]) was obtained as light yellow oily matter at 159mg and 95.5% of yield.

[0039] ¹HNMR(400MHz and CDCl₃);delta1.03 (d, J= 6.8Hz, 6H), 1.15(s,6H),1.27(d,J=6.8Hz,6H),2.36 (sept,J=6.8Hz,1H), 2.58(s,2H),3.09(sept,J=6.8Hz,1H), 4.93(broad s,1H),6.68(dd,J=8.3 and 2.4Hz,1H), 6.80 (d,J=2.4Hz,1H),6.95(d,J=8.3Hz,1H)ppmIR(liq.film);3370,2960,1705,1580cm⁻¹Mass(m/z,%);274(M+ ,6), 273 (37),258(49),2 [30 (100) and 174] (67), 160 (16), 146 (25)

[0040] (Example 9 of reference)

[Formula 18]

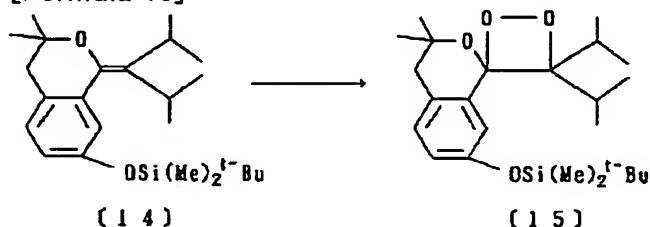


anhydrous in compound [13] 121mg (0.442mmol) compounded in the example 8 of reference — it dissolved in DMF 5ml and stirred at 0 degree C under nitrogen atmosphere Triethylamine 2.0ml (14.3mmol) and t-butyldimethyl chlorosilane 100mg (0.663mmol) were added to this solution, and it stirred at the room temperature for 2 hours. Reaction mixture was invested in water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by 10:1 mixed solvents of a hexane and ethyl acetate, it is 7-t-butyldimethylsiloxy-1-diisopropyl methylidyne. — The 3 and 3-dimethyl iso chroman (compound [14]) was obtained as colorless oily matter at 138mg and 80.5% of yield.

[0041] ¹H NMR (400MHz and CDCl₃); delta 0.19 (s, 6H), 0.99 (s, 9H), 1.03 (d, J=6.8Hz, 6H), 1.14 (s, 6H), 1.27 (d, J=6.8Hz, 6H), 2.35 (sept, J=6.8Hz, 1H), 2.58 (s, 2H), 3.09 (sept, J=6.8Hz, 1H), 6.70 (dd, J=7.8 and 2.4Hz, 1H), 6.81 (d, J=2.4Hz, 1H), 6.94 (d, J=7.8Hz, 1H) ppm IR (liq. film); 2960, 2860, 1580, 1470, 1270 cm⁻¹ Mass (m/z, %); 388 (M⁺, 56), 373 (85), 345 (83), 288 (27), 234 (24), 220 (50), 206 (41), 73 (100)

[0042] (Example 3)

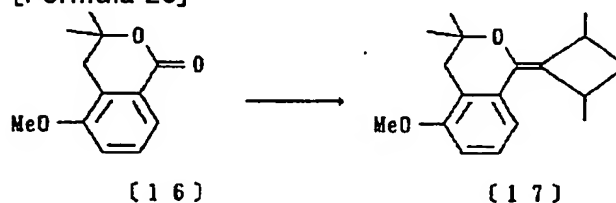
[Formula 19]



Compound [14] 85mg (0.219mmol) compounded in the example 9 of reference and TPP 5mg were dissolved in dichloromethane 10ml, and it stirred at -78 degrees C under oxygen atmosphere. The sodium lamp (940W) performed optical irradiation in this solution for 2 hours. The reaction mixture was condensed, and applied to a silica gel column, and it began to pass by the mixed solvent of 10:1 of a hexane and ethyl acetate — 7 — t-butyldimethylsiloxy-4,4-diisopropyl-3,3-dimethyl SUPIRO [1,2-JIOKI cetane-3, and 1'-iso chroman] (compound [15]) was obtained as light yellow oily matter at 56mg and 60.9% of yield

[0043] ¹H NMR (400MHz and CDCl₃); delta 0.23 (s, 6H), 0.46 (d, J=7.3Hz, 3H), 0.78 (d, J=7.3Hz, 3H), 0.91 (s, 3H), 1.00 (s, 9H), 1.16 (d, J=7.3Hz, 3H), 1.33 (d, J=7.3Hz, 3H), 1.48 (s, 3H), 2.61 (sept, J=7.3Hz, 1H), 2.63 (qAB, J=5.0Hz, 2H), 2.97 (sept, J=7.3Hz, 1H), 6.86 (dd, J=8.3 and 2.4Hz, 1H), 6.95 (d, J=8.3Hz, 1H), 7.73 (d, J=2.4Hz, 1H) ppm IR (liq. film); 2935, 1610 and 1495, 1285 cm⁻¹. [0044] (Example 10 of reference)

[Formula 20]

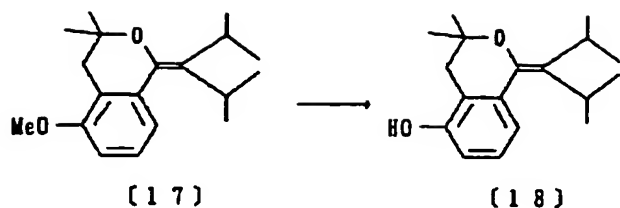


anhydrous [in 4.5g (29.2mmol) of titanium trichlorides] at the bottom of nitrogen atmosphere, and 0 degree C — lithium-hydride aluminum 570mg (15.0mmol) was added to the solution suspended in THF 75ml, and it stirred at the room temperature Triethylamine 2.10ml (15.1mmol) was added to this solution, and heating reflux was carried out for 15 minutes. anhydrous [in 5-methoxy-3 and 3-dimethyl iso chroman-1-ON (compound [16]) 618mg (3.00mmol) and diisopropyl keton 1.8ml (12.7mmol)] in this solution — it dissolved in THF 25ml, and it applied for 20 minutes, and was dropped, and heating reflux was carried out for further 1 hour Reaction mixture was invested in iced water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with water. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 3:1 of a hexane and a dichloromethane, the 1-diisopropyl methylidyne-5-methoxy-3 and the 3-dimethyl iso chroman (compound [17]) were obtained as colorless oily matter at 620mg and 71.8% of yield.

[0045] ¹H NMR (400MHz and CDCl₃); delta 1.02 (d, J= 6.8Hz, 6H), 1.17 (s, 6H), 1.28 (d, J=6.8Hz, 6H), 2.36 (sept, J=6.8Hz, 1H), 2.69 (s, 2H), 3.07 (sept, J=6.8Hz, 1H), 3.83 (s, 3H), 6.78 (d, J=7.8Hz, 1H), 6.95 (d, J=7.8Hz, 1H), 7.15 (t, J=7.8Hz, 1H) ppm IR (liq. film); 2985, 2870, 1580, 1475, 1365, 1265, 1130 cm⁻¹ Mass (m/z, %); 288 (M⁺, 18), 273 (41), 245 (37), 189 (39), 161 (25), 149 (100)

[0046] (Example 11 of reference)

[Formula 21]

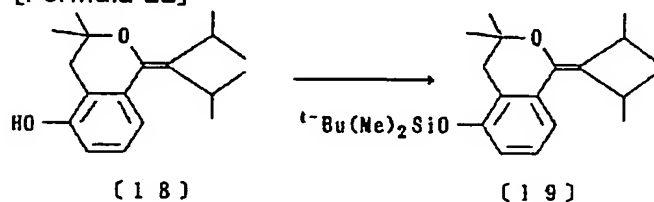


anhydrous in 80mg (2.00mmol) of 60% sodium hydrides — it suspended in DMF2ml, ethanethiol 0.15ml (2.03mmol) was added to the solution stirred at 0 degree C under argon atmosphere, and it stirred for 20 minutes anhydrous in compound [17] 215mg (0.746mmol) compounded in the example 10 of reference in this solution — it dissolved in DMF1ml and, in addition, heating reflux was carried out for 3 hours Reaction mixture was invested in saturation brine and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of a hexane and ethyl acetate 5:1, it is 1-diisopropyl methylidyne-5-hydroxy. — The 3 and 3-dimethyl iso chroman (compound [18]) was obtained as light yellow oily matter at 136mg and 66.5% of yield.

[0047] ¹HNMR(300MHz and CDCl₃);delta1.02 (d, J= 6.8Hz, 6H), 1.19(s,6H),1.28(d,J=6.8Hz,6H),2.36 (sept,J=6.8Hz,1H), 2.67(s,2H),3.07(sept,J=6.8Hz,1H), 4.68(broad s,1H),6.69(d,J=7.8Hz,1H), 6.93 (d,J=7.8Hz,1H),7.06(t,J=7.8Hz,1H)ppmIR(liq.film);3400,2960,2870,1655,1580cm⁻¹Mass(m/z,%);274(M+ ,52),259(54),231(78), 175(10 [0 and 147] (21), 135 (46)

[0048] (Example 12 of reference)

[Formula 22]



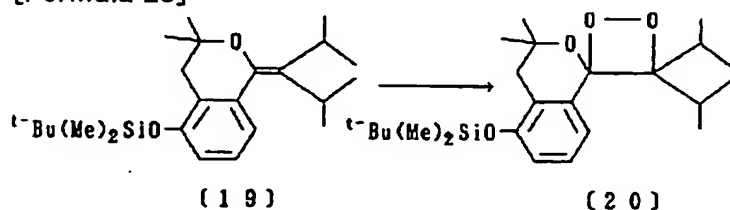
anhydrous in compound [18] 130mg (0.474mmol) compounded in the example 11 of reference — it dissolved in DMF5ml and stirred at 0 degree C under nitrogen atmosphere Triethylamine 2.0ml (14.3mmol) and t-butyldimethyl chlorosilicane 100mg (0.663mmol) were added to this solution, and it stirred at the room temperature for 2 hours. Reaction mixture was invested in water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by 10:1 mixed solvents of a hexane and ethyl acetate, it is 5-t-butyl(dimethyl)siloxy-1-diisopropyl methylidyne. — The 3 and 3-dimethyl iso chroman (compound [19]) was obtained at 142mg and 77.1% of yield.

[0049] Melting point; 88.0 to 89.0 degree C (it recrystallizes with a colorless needle shape crystal, and a hexane and ethyl acetate)

¹HNMR(400MHz and CDCl₃);delta0.21 (s, 6H), 1.01(d,J=6.8Hz,6H),1.01(s,9H),1.16(s,6H), 1.27 (d,J=6.8Hz,6H),2.36(sept,J=6.8Hz,1H), 2.66(s,2H),3.07(sept,J=6.8Hz,1H), 6.72(d,J=7.8Hz,1H),6.93 (d,J=7.8Hz,1H), 7.04(d,J=7.8Hz,1H)ppmIR(KBr);2960,2860,1580,1470,1270cm⁻¹Mass(m/z,%);388(M+ ,69),373(88),345(100, 289 (37)

[0050] (Example 4)

[Formula 23]

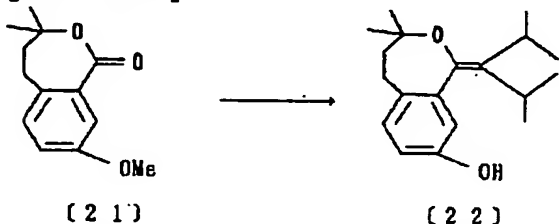


Compound [19] 51mg (0.131mmol) compounded in the example 12 of reference and TPP5mg were dissolved in dichloromethane 10ml, and it stirred at -78 degrees C under oxygen atmosphere. The sodium lamp (940W) performed optical irradiation in this solution for 2 hours. the place which condenses reaction mixture, and applies a concentrate to a silica gel column, and it began to pass by the mixed solvent of 10:1 of a hexane and ethyl acetate — 5 — t-butyl(dimethyl)siloxy -4, 4-diisopropyl-3', 3' - dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' - iso chroman] (compound [20]) was obtained as light yellow oily matter at 30mg and 54.3% of yield

[0051] ¹HNMR(400MHz and CDCl₃);delta 0.18 (s, 3H), 0.19(s,3H),0.46(d,J=7.3Hz,3H),0.74(d,J=7.3Hz,3H), 0.92(s,3H),1.00(s,9H),1.15(d,J=7.3Hz,3H), 1.33(d,J=7.3Hz,3H),1.51(s,3H),2.66(qAB,J=15.3Hz,2H), 2.54 (sept,J=7.3Hz,1H),2.98(sept,J=7.3Hz,1H), 6.89(d with fine coupling,J=7.8Hz,1H), 7.25(t,J=7.8Hz,1H),7.90(d, J= 7.8Hz, 1H) ppmIR(liq.film); — 2930, 1470, and 1255cm⁻¹Mass(m/z, %);388 (32 M+ 7) — 191 (100) 306 (38), 249 (35), 163 (17)

[0052] (Example 13 of reference)

[Formula 24]



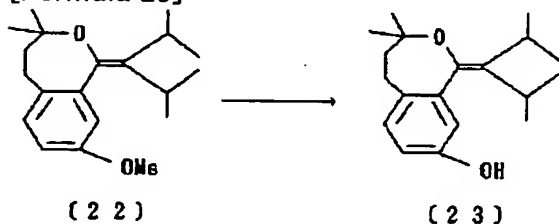
anhydrous in the bottom of argon atmosphere, and 5.0g (32.4mmol) of titanium trichlorides -- after suspending in THF100ml and stirring for 15 minutes, it ice-cooled, lithium-hydride aluminum 629mg (16.6mmol) was added, and it stirred for 30 minutes at the room temperature Triethylamine 2.30ml (16.5mmol) was added to this solution, and heating reflux was carried out for 30 minutes. anhydrous [in 8-methoxy -3 and 3-dimethyl-2-benzo OKISEPAN-1-ON (compound [21]) 695mg (3.16mmol) and diisopropyl keton 0.95ml (6.71mmol)] in this solution -- it dissolved in THF20ml, and it applied for 30 minutes, and was dropped, and heating reflux was carried out for further 1 hour Reaction mixture was invested in iced water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness one by one with water, sodium-hydrogencarbonate solution, and saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of 20:1 of a hexane and ethyl acetate, 1-diisopropyl methylidyne-8-methoxy -3 and 3-dimethyl-2-benzo OKISEPAN (compound [22]) was obtained at 128mg and 13.4% of yield.

[0053] Melting point; 55.0 to 56.0 degree C (it recrystallizes from a colorless needle shape crystal and a methanol)

¹HNMR(300MHz and CDCl₃);delta 0.96 (d, J= 6.8Hz, 6H), 1.07(broad s,6H),1.26(d,J=7.0Hz,6H), 1.76-1.94 (m,2H),2.59(sept,J=7.0Hz,1H), 2.67(sept,J=6.8Hz,1H),2.27-2.86(m,2H), 3.78(s,3H),6.71-6.78(m,2H),7.00 (d,J=9.2Hz,1H)ppmIR(KBr);2968,2928,2864,1616,1574cm⁻¹Mass(m/z,%);302(M+ ,61),259(100), 231(14),204 (28),203 (89), 189 (37), 175 (34), 161 (20)

[0054] (Example 14 of reference)

[Formula 25]

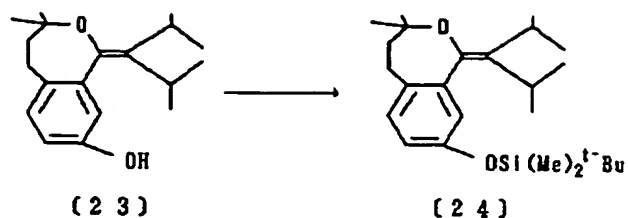


anhydrous in compound [22] 89mg (0.295mmol) compounded 60% in 30mg (0.750mmol) of sodium hydrides, and the example 13 of reference -- it suspended in DMF1.75ml, ethanethiol 0.06ml (0.810mmol) was added to the solution stirred at 0 degree C under argon atmosphere, and it stirred for 15 minutes at the room temperature Heating stirring of this solution was continuously carried out for 30 minutes per hour at 150 degrees C by 130 degrees C for 3 hours. Reaction mixture was invested in saturation brine and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by the mixed solvent of a hexane and ethyl acetate 10:1, it is 1-diisopropyl methylidyne-8-hydroxy. - 3 and 3-dimethyl-2-benzo OKISEPAN (compound [23]) was obtained as a colorless indeterminate form solid-state at 45mg and 53.0% of yield.

[0055] ¹HNMR(300MHz and CDCl₃);delta 0.95 (d, J= 6.9Hz, 6H), 1.07(broad s,6H),1.25(d,J=7.1Hz,6H), 1.78-1.90(m,2H),2.58(sept,J=7.1Hz,1H), 2.66(sept,J=6.9Hz,1H),2.70-2.84(m,2H), 4.54(s,1H),6.63-6.70 (m,2H),6.96(d,J=7.8Hz,1H)ppmIR(KBr);3400,2960,2932,2872,1712,1608,1580cm⁻¹Mass(m/z,%);288(M+ ,66), 245(100),217(14),1 [89] (85), 175 (28), 161 (32), 147 (18)

[0056] (Example 15 of reference)

[Formula 26]

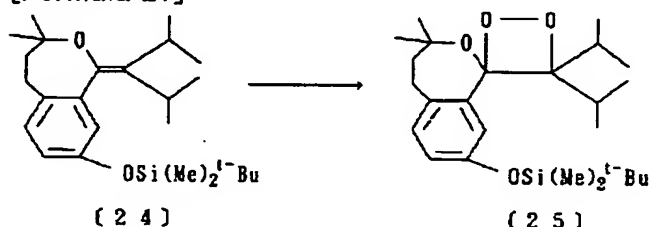


anhydrous in compound [23] 43mg (0.15mmol) compounded in the example 14 of reference — it dissolved in DMF 1.5ml and stirred at the bottom room temperature of argon atmosphere Imidazole 28mg (0.41mmol) and *t*-butyldimethyl chlorosilane 51mg (0.34mmol) were added to this solution, and it stirred at the room temperature overnight. Reaction mixture was invested in water and ethyl acetate extracted. The extract layer was condensed after washing and magnesium sulfate dryness with saturation brine. When applying a concentrate to a silica gel column and having begun to pass by 20:1 mixed solvents of a hexane and the ether, it is 8-*t*-butyldimethylsiloxy-1-diisopropyl methylidyne. — 3 and 3-dimethyl-2-benzo OKISEPAN (compound [24]) was obtained as colorless oily matter at 52mg and 82.6% of yield.

[0057] ¹H NMR (300MHz and CDCl₃); δ 0.16 (s, 6H), 0.94 (d, J=6.9Hz, 6H), 0.97 (s, 9H), 0.86–1.10 (m, 6H), 1.26 (d, J=7.0Hz, 6H), 1.78–1.90 (m, 2H), 2.50 (sept, J=7.0Hz, 1H), 2.68 (sept, J=6.9Hz, 1H), 2.68–2.84 (m, 2H), 6.66–6.72 (m, 2H), 6.95 (d, J=8.6Hz, 1H) ppm IR (liq. film); 2960, 2932, 2864, 1606, 1572, 1288 cm⁻¹ Mass (m/z, %); 403 (M⁺ +1, 25), 402 (M⁺, 76), 360 (29), 359 (100) and 304 (32), 303 (80), 289 (34)

[0058] (Example 5)

[Formula 27]



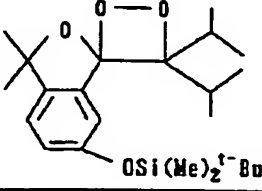
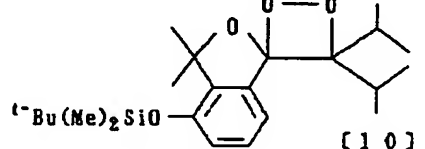
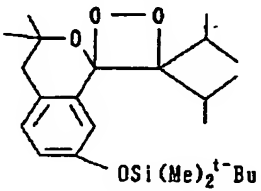
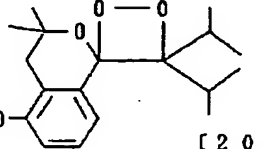
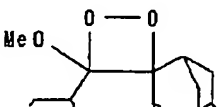
Compound [24] 48mg (0.12mmol) compounded in the example 15 of reference and TPP 4mg were dissolved in dichloromethane 20ml, and it stirred at -78 degrees C under oxygen atmosphere. The sodium lamp (180W) performed optical irradiation in this solution for 3 hours. the place which condenses reaction mixture, and applies a concentrate to a silica gel column, and it began to pass by the mixed solvent of 20:1 of a hexane and the ether — 8 — *t*-butyldimethylsiloxy -4, 4-diisopropyl-3', 3'-dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' - (2'-benzo OKISEPAN)] (compound [25]) was obtained as a colorless indeterminate form solid-state at 45mg and 86.8% of yield

[0059] ¹H NMR (300MHz and CDCl₃); δ 0.21 (s, 6H), 0.53 (d, J=7.1Hz, 3H), 0.75 (d, J=7.0Hz, 3H), 0.85 (s, 3H), 0.99 (s, 9H), 1.25 (d, J=7.1Hz, 3H), 1.38 (s, 3H), 1.45 (d, J=7.0Hz, 3H), 1.65 (td, J=13.1 and 4.4Hz, 1H), 2.00 (ddd, J=13.1, 5.3 and 2.6Hz, 1H), 2.32 (sept, J=7.1Hz, 1H), 2.41 (ddd, J=13.4, 4.4 and 2.6Hz, 1H), 2.77 (sept, J=7.0Hz, 1H), 3.09 (td, J=13.4 and 5.3Hz, 1H), 6.80 (dd, J=8.1 and 2.6Hz, 1H), 6.93 (d, J=8.1Hz, 1H), 7.59 (d, J=2.6Hz, 1H) ppm IR (KBr); 2968, 2936 and 1608, 1274 cm⁻¹ Mass (m/z, %); 434 (M⁺, 0.1), 207 (100) 402 (38), 359 (17), 320 (42), 263 (24), 205 (19)

[0060] (Example 1 of an examination) Set in the examples 1, 2, 3, and 4. 6 obtained — *t*-butyldimethylsiloxy-1', 3'-dihydro-4, and 4-diisopropyl-3', 3'-dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' - iso benzofuran] (compound [5]) — 4 — *t*-butyldimethylsiloxy-1', 3'-dihydro-4, and 4-diisopropyl-3', 3'-dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' - iso benzofuran] (compound [10]) — 7 — *t*-butyldimethylsiloxy -4, 4-diisopropyl-3', 3'-dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' - iso chroman] (compound [15]) and 5 — *t*-butyldimethylsiloxy -4 and the 4-diisopropyl -3' — 3'-dimethyl SUPIRO [1, 2-JIOKI cetane -3, and 1' — 1.8x10⁻⁵M of - iso chroman] (compound [20]) 1ml of DMSO solutions It is 1.0x10⁻³M of tetrabutylammoniumfluoride, respectively. It added to 2ml of DMSO solutions at 25 degrees C, and luminescence at that time was measured with the fluorometric analysis plan. The quantum yield and half-life of luminescence at this time were shown in the table. In addition, as comparison, 4-(3-*t*-butyldimethyl silyloxy phenyl)-4-methoxy SUPIRO [1, 2-JIOKI cetane -3, and 2'-adamantane] were also measured on the same measurement conditions, and the half-life of luminescence was shown in the table.

[0061]

[Table 1]

化 合 物	化学発光 量子収率	λ_{max}	化学発光 の半減期 (秒)
 OSi(Me) ₂ ^t -Bu (5)	0.15	456	153
 ^t -Bu(Me) ₂ SiO (1 0)	>0.12	438	3329
 OSi(Me) ₂ ^t -Bu (1 5)	>0.10	486	4520
 ^t -Bu(Me) ₂ SiO (2 0)	0.28	472	23.5
 MeO	(2 5)	463 (2 5)	4.7 (2 5)

$t\text{-Bu(Me)}_2\text{SiO}-$ 		(0.65)	(0.10)	(3.0)
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()内はA. P. Schaap, et al., Tetrahedron Lett., 28, 1155(1987)参照

[0062]

[Effect of the Invention] As for 1 of this invention, and 2-JIOKI cetane derivative (I), luminescence durability has the feature that it is remarkable and is long. That is, the stable measurement data is obtained and after a luminescence start brings a high result of repeatability, in order that stable luminescence may continue.

[Translation done.]

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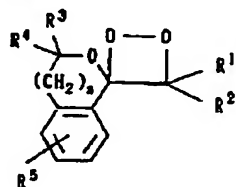
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最終頁に続く

(54) 【発明の名称】 オキサベンゾシクロアルケン環とスピロ結合した1, 2-ジオキセタン誘導体

(57) 【要約】 (修正有)

【解決手段】 下記式



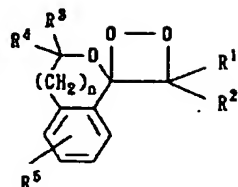
で表される1, 2-ジオキセタン誘導体(式中、 R^1 、 R^2 、 R^3 及び R^4 は水素原子、低級アルキル基又はアリール基である。また、 R^1 と R^2 及び R^3 と R^4 は一体となり、環状アルキル基を形成することもある。 R^5 はヒドロキシル基、低級アルコキシ基、アラルキルオキシ基、 $-\text{OSi}(R^6 R^7 R^8)$ (ただし、 R^6 、 R^7 及び R^8 は互いに独立に低級アルキル基である)又はリン酸塩基である。)

【効果】 上記の新規な1, 2-ジオキセタン誘導体は、化学発光試薬として免疫測定等に使用することができる。

【特許請求の範囲】

【請求項1】 一般式

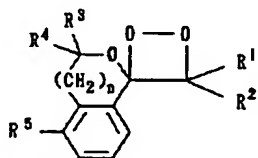
【化1】



で表される1, 2-ジオキセタン誘導体(式中、 R^1 、 R^2 、 R^3 及び R^4 は水素原子、アルキル基又はアリール基である。また、 R^1 と R^2 及び R^3 と R^4 は一体となり、環状アルキル基を形成することもできる。 R^5 はヒドロキシル基、アルコキシル基、アラルキルオキシ基、 $-\text{OSi}(R^6, R^7, R^8)$ (ただし R^6 、 R^7 及び R^8 は互いに独立にアルキル基である。)又はリン酸塩基である。 n は0、1又は2である。)

【請求項2】 一般式

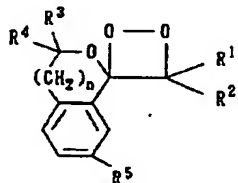
【化2】



で表される請求項1に記載の1, 2-ジオキセタン誘導体。

【請求項3】 一般式

【化3】



で表される請求項1に記載の1, 2-ジオキセタン誘導体。

【請求項4】 R^1 、 R^2 、 R^3 及び R^4 がアルキル基である請求項1に記載の1, 2-ジオキセタン誘導体。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】本発明は、新規な1, 2-ジオキセタン誘導体に関する。本発明の1, 2-ジオキセタン誘導体は化学発光試薬として免疫測定等に使用することができる。

【0002】

【従来の技術】従来より、1, 2-ジオキセタン誘導体は種々合成されており、特に3位にスピロアダマンチル基が結合した化合物は化学発光基質として有用であることが知られている(例えば、特公平5-21918号公報明細書及び特公平5-45590号公報明細書参照)。

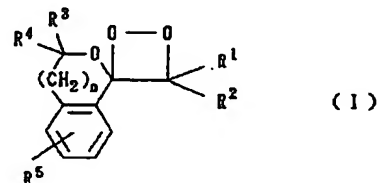
【0003】

【発明が解決しようとする課題】しかしながら、従来の化合物は発光持続性に対して十分な効果があるとは言えず、その改良が望まれていた。

【0004】

【課題を解決するための手段】本願発明者は、従来の化合物の持つ欠点を克服すべく鋭意検討した結果、一般式(1)

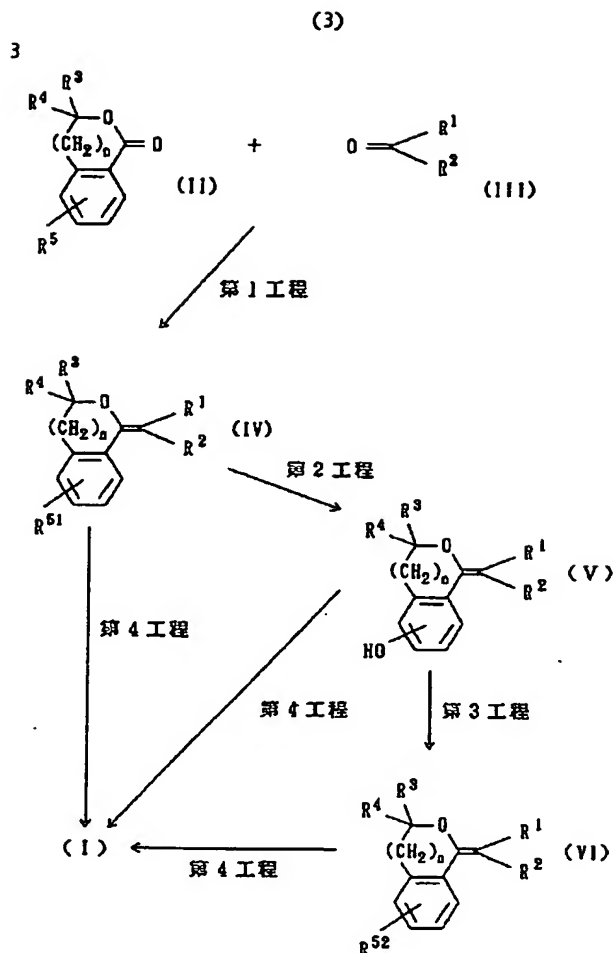
20 【化4】



(式中、 R^1 、 R^2 、 R^3 及び R^4 は水素原子、アルキル基又はアリール基である。また、 R^1 と R^2 及び R^3 と R^4 は一体となり、環状アルキル基を形成することもできる。 R^5 はヒドロキシル基、アルコキシル基、アラルキルオキシ基、 $-\text{OSi}(R^6, R^7, R^8)$ (ただし、 R^6 、 R^7 及び R^8 は互いに独立にアルキル基である。)又はリン酸塩基である。 n は0、1又は2である。)で表される1, 2-ジオキセタン誘導体を見出し本発明を完成したものである。

【0005】本発明の前記一般式(1)で表される1, 2-ジオキセタン誘導体は以下の反応式に従い製造することができる。

【化5】



〔式中、 $R^1 \sim R^4$ は前記と同じである。 R^{51} はアルコキシ基又はアラルキルオキシ基であり、 R^{52} は $-\text{OSi}(R^5 R^6 R^7)$ ($R^5 \sim R^7$ は前記と同じである。) 又はリン酸塩基である。〕

〔0008〕以下、本発明を詳細に説明するにあたって、本発明で「アルキル基」とは、置換基を有してもよい炭素数1～20個の直鎖状又は分枝鎖状のアルキル基をいい、そのアルキル基は、メチル、エチル、プロピル、ブチル、ペンチル、ヘキシル、ヘプチル、オクチル、ノニル、デシル、ウンデシル、ドデシル、テトラデシル、ペンタデシル、ヘキサデシル、ヘプタデシル、オクタデシル、ノナデシル、イコデシルの直鎖の基及び前記のアルキル基が適宜分枝状に結合した基をいう。前記置換してもよい基とは、例えば、ヒドロキシ基、アルコキシ基、アリール基、複素環基等である。そのアルコキシ基としては、例えば、メトキシ、エトキシ、プロポキシ、ブトキシ、ペンチルオキシ、ヘキシルオキシ、メトキシエトキシ、メトキシプロポキシ、エトキシエトキシ、エトキシプロポキシ、メトキシエトキシエトキシ等であり、またそのアリール基としては、例えば、フェニル、ナフチル基等であり、その複素環基としては、フリル、チエニル、ビリジル基等である。

〔0007〕また、本発明で「アルコキシ基」とは、前記したアルキル基に置換してもよいアルコキシ基と同じであり、「アリール基」とは、フェニル、ナフチル基等の芳香族炭化水素基及び環内に窒素、酸素あるいは硫黄原子を有するヘテロアリール基を指すものである。さらに「アラルキルオキシ基」とはベンジルオキシ基、フェネチルオキシ基等である。

〔0008〕(第1工程) 本工程は、一般式(II)で表される二環式ラクトンと一般式(III)で表されるケトンとを反応させ、一般式(IV)で表されるアルケン誘導体を製造するものである。

〔0009〕反応はチタンの存在下に行うことを必須の要件とし、チタンとしては塩化チタン等のハロゲン化チタンを用いることが好ましい。

〔0010〕また、還元剤としては、水素化リチウムアルミニウム等、塩基としてはトリエチルアミン、ピリジン等を用いて還元状態を形成させ、反応に供することが望ましい。

〔0011〕反応を行うにあたってはテトラヒドロフラン (THF) 等の有機エーテル中で行うことができる。

〔0012〕反応は0～100℃で進行するが、THFの回流下に行うことが操作及び反応性の観点から好まし

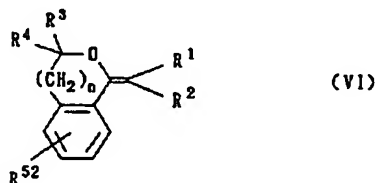
い。

【0013】(第2工程)本工程は、前記一般式(IV)で表される化合物の脱保護反応を行い一般式(V)で表されるアルコール誘導体を製造するものである。

【0014】脱保護反応に供する化合物としては前記一般式(IV)($R^1 \sim R^4$ は前記と同じであり、 $R^{1'}$ は水酸基の保護基(好ましくはメトキシ基、ベンジルオキシ基である。))であり、反応は当業者に熟知された方法、即ちアルキルチオールのアニオンを反応させ行うか或いは水素添加反応に付すことにより行うことができるが、どちらの反応を選択するかは脱保護すべき基により適宜選択すればよい。

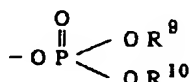
【0015】(第3工程)本工程は前記一般式(V)で表される化合物にシリルオキシ基或いはリン酸基形成のため対応するハロゲン化トリアルキルシラン或いはハロゲン化ホスフェートを反応させ、一般式(VI)

【化6】



(式中、 $R^1 \sim R^4$ は前記と同じであり、 $R^{1'}$ は $-\text{OSi}(R^5 R^6 R^7)$ ($R^5 \sim R^7$ は前記と同じである。)又は

【化7】



である。 R^8 及び R^{10} はアルキル基或いは R^9 、 R^{10} が一体となり環を形成してもよい基である。)で表される化合物を製造するものである。

【0016】さらに本工程において、例えばリン酸基導入のためクロロエチレンホスフェートを反応させた場合は、シアン化ナトリウムでシアノエチルホスフェートのナトリウム塩に変換し、さらにシアノエチル基を脱離し、アンモニウムナトリウム塩に変換することができる。このアンモニウムナトリウム塩は、例えば炭酸水素ナトリウムと反応させることにより容易にジナトリウム塩に変換できる。

【0017】(第4工程)本工程は一般式(IV)、(V)又は(VI)で表されるアルケン誘導体を一重項酸素と反応させ、前記一般式(1)で表される1,2-ジオキセタン誘導体を製造するものである。

【0018】一重項酸素との反応は、前記一般式(IV)、(V)又は(VI)で表されるアルケン誘導体をジクロロメタン、ジクロロエタン、四塩化炭素等のハロゲン化炭化水素又はメタノール、エタノール等のアルコール等の溶媒に溶解し、メチレンブルー、ローズベンガル、テトラ

フェニルボルフィン等の光増感剤の共存下、酸素雰囲気の下で可視光照射を行うことにより達成される。なお、反応は -80°C ～室温で行うものである。

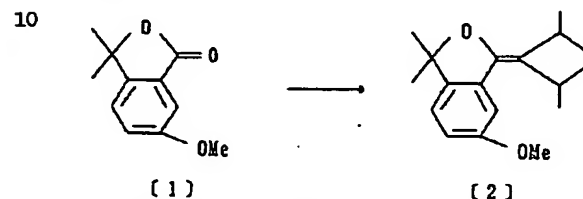
【0019】以下、実施例及び参考例により本発明を詳細に説明する。

【0020】

【実施例】

(参考例1)

【化8】



アルゴン雰囲気下、三塩化チタン5.3g(34.4mmol)を無水THF100mlに懸濁して15分間攪拌した後、氷冷して水素化リチウムアルミニウム660mg(17.4mmol)を加え、室温で30分間攪拌した。この溶液にトリエチルアミン2.4ml(17.2mmol)を加え、30分間加熱還流した。この溶液に6-メトキシ-1,3-ジヒドロ-3,3-ジメチルイソベンゾフラン-1-オン(化合物(1))655mg(3.41mmol)及びジイソプロピルケトン1.0ml(7.06mmol)を無水THF20mlに溶解し45分間かけて滴下し、さらに1時間加熱還流した。反応混合物を氷水に投じ酢酸エチルで抽出した。抽出層を、水、炭酸水素ナトリウム水溶液及び飽和食塩水で順次洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの20:1の混合溶媒で流しだしたところ、1-ジイソプロピルメチリデン-1,3-ジヒドロ-6-メトキシ-3,3-ジメチルイソベンゾフラン(化合物(2))が497mg、収率53.6%で得られた。

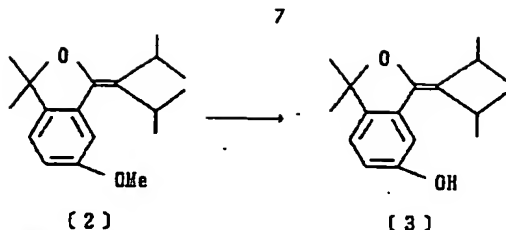
【0021】融点: $86.0 \sim 87.0^\circ\text{C}$ (無色板状晶、メタノールより再結晶)

$^1\text{H NMR}$ (300MHz, CDCl_3): δ 1.10(d, $J=6.9\text{Hz}$, 6H), 1.25(d, $J=7.0\text{Hz}$, 6H), 1.48(s, 6H), 2.45(sept, $J=7.0\text{Hz}$, 1H), 3.33(sept, $J=6.9\text{Hz}$, 1H), 3.82(s, 3H), 6.79(dd, $J=8.3$ and 2.2Hz , 1H), 7.04(d, $J=8.3\text{Hz}$, 1H) and 7.14(d, $J=2.2\text{Hz}$, 1H) ppm
IR(KBr): 2960, 2932, 1648, 1616 and 1584cm^{-1}

Mass(m/z , %): 274(M^+ , 35), 259(100) and 231(24)

【0022】(参考例2)

【化9】



60%水酸化ナトリウム80mg (2.00mmol) を無水DMF 2mlに懸濁しアルゴン雰囲気下、0℃で攪拌した溶液にエタントール0.15ml (2.03mmol)を加え20分間攪拌した。この溶液に参考例1で合成した化合物〔2〕150mg (0.547mmol)を無水DMF 1mlに溶解して加え、3時間加熱還流した。反応混合物を飽和食塩水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの5:1の混合溶媒で流しだしたところ、1-ジイソプロピルメチリデン-1,3-ジヒドロ-6-ヒドロキシ-3,3-ジメチルイソベンゾフラン (化合物〔3〕)が135mg、収率94.9%で無色粘稠物として得られた。

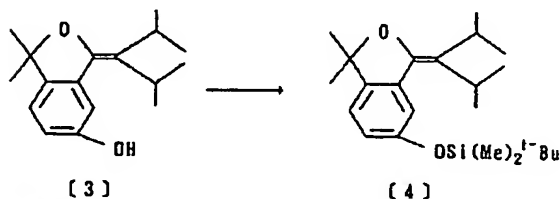
〔0023〕¹HNMR (400MHz, CDCI₃) : δ 1.09 (d, J=6.8Hz, 6H), 1.25 (d, J=6.8Hz, 6H), 1.25 (s, 6H), 2.44 (sept, J=6.8Hz, 1H), 3.29 (sept, J=6.8Hz, 1H), 4.81 (broad s, 1H), 6.70 (dd, J=7.8 and 2.4Hz, 1H), 6.98 (d, J=7.8Hz, 1H), 7.08 (d, J=2.4Hz, 1H) ppm

IR (liq. film) : 3385, 2970, 1735, 1610 cm⁻¹

Mass (m/z, %) : 260 (M⁺, 22), 245 (100), 217 (39), 205 (63), 163 (37)

〔0024〕 (参考例3)

〔化10〕



参考例2で合成した化合物〔3〕130mg (0.500mmol)を無水DMF 2mlに溶解し、アルゴン雰囲気下0℃で攪拌した。この溶液にトリエチルアミン1.0ml (7.17mmol)及びt-ブチルジメチルクロロシラン0.10g (0.663mmol)を加え室温で1時間攪拌した。反応混合物を水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムに

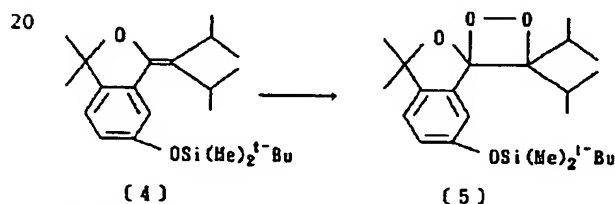
かけ、ヘキサンと酢酸エチルの10:1の混合溶媒で流しだしたところ、6-t-ブチルジメチルシロキシ-1-ジイソプロピルメチリデン-1,3-ジヒドロ-3,3-ジメチルイソベンゾフラン (化合物〔4〕)が152mg、収率81.3%で無色油状物として得られた。

〔0025〕¹HNMR (400MHz, CDCI₃) : δ 0.21 (s, 6H), 0.99 (s, 9H), 1.10 (d, J=6.8Hz, 6H), 1.25 (d, J=6.8Hz, 6H), 1.47 (s, 6H), 2.45 (sept, J=6.8Hz, 1H), 3.28 (sept, J=6.8Hz, 1H), 6.70 (dd, J=7.8 and 2.0Hz, 1H), 6.95 (d, J=7.8Hz, 1H), 7.05 (d, J=2.0Hz, 1H) ppm

IR (KBr) : 2955, 1610, 1285 cm⁻¹
Mass (m/z, %) : 374 (M⁺, 32), 259 (100), 331 (15)

〔0026〕 (実施例1)

〔化11〕

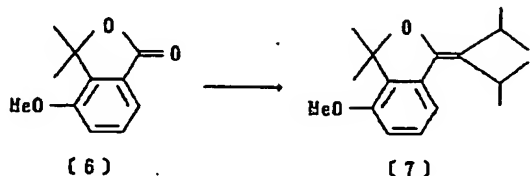


参考例3で合成した化合物〔4〕100mg (0.267mmol)及びTPP 5mgをジクロロメタン10mlに溶解し、酸素雰囲気下-78℃で攪拌した。この溶液にナトリウムランプ (940W) で2時間光照射を行った。反応混合物を濃縮し、濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの10:1の混合溶媒で流しだしたところ、6'-t-ブチルジメチルシロキシ-1',3'-ジヒドロ-4,4-ジイソプロピル-3',3'-ジメチルスピロ〔1,2-ジオキセタン-3,1'-イソベンゾフラン〕 (化合物〔5〕)が97mg、収率89.4%で淡黄色油状物として得られた。

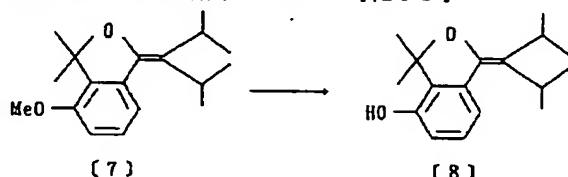
〔0027〕¹HNMR (400MHz, CDCI₃) : δ 0.22 (s, 3H), 0.23 (s, 3H), 0.74 (d, J=7.3Hz, 3H), 0.99 (d, J=7.3Hz, 3H), 1.01 (s, 9H), 1.18 (d, J=7.3Hz, 3H), 1.35 (d, J=7.3Hz, 3H), 1.47 (s, 3H), 1.55 (s, 3H), 2.89 (sept, J=7.3Hz, 1H), 3.08 (sept, J=7.3Hz, 1H), 6.92 (dd, J=8.3 and 2.4Hz, 1H), 6.99 (d, J=8.3Hz, 1H), 7.39 (d, J=2.4Hz, 1H) ppm

IR (liq. film) : 2965, 2860, 1255 cm⁻¹

Mass (m/z, %): 374 (M⁺, 32.1), 259 (17), 292 (22), 235 (100), 217 (11)
 [0028] (参考例4)
 [化12]



アルゴン雰囲気下、三塩化チタン5.0mg (32.4 mmol) を無水THF 100ml に懸濁して15分間攪拌した後、氷冷して水素化リチウムアルミニウム632mg (16.7 mmol) を加え、室温で30分間攪拌した。この溶液にトリエチルアミン2.3ml (16.5 mmol) を加え、30分間加熱還流した。この溶液に1,3-ジヒドロ-4-メトキシ-3,3-ジメチルイソベンゾフラン-1-オン (化合物〔6〕) 625mg (3.26 mmol) 及びジイソプロピルケトン 200.96ml (6.78 mmol) を無水THF 20ml に溶解し10分間かけて滴下し、さらに1時間加熱還流した。反応混合物を氷水に投じ酢酸エチルで抽出し *



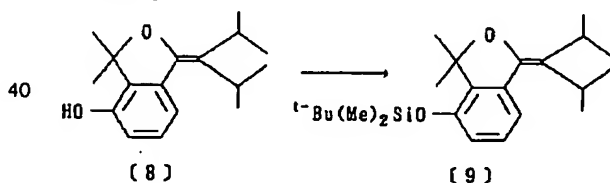
60%水素化ナトリウム126mg (3.15 mmol) 及び参考例4で合成した化合物〔7〕371mg (1.36 mmol) を無水DMF 4.5ml に懸濁し、アルゴン雰囲気下0℃で攪拌した溶液に、エタノール0.22ml (2.97 mmol) を加え10分間攪拌した。この溶液を2時間加熱還流した。反応混合物を飽和食塩水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの混合溶媒で流したところ、1-ジイソプロピルメチリデン-1,3-ジヒドロ-4-ヒドロキシ-3,3-ジメチルイソベンゾフラン (化合物〔8〕) が335mg、収率95.2%で得られた。
 [0031] 融点: 98.0-98.5℃ (無色粒状晶、ヘキサンより再結晶)

¹H NMR (300MHz, CDCl₃); δ 1.09 (d, J=6.8 Hz, 6H), 1.26 (d, J=7.0 Hz, 6H), 1.60 (s, 6H), 2.44 (sept, J=7.0 Hz, 1H), 3.36 (sept, J=6.8 Hz, 1H), 4.65 (s, 1H), 6.57 (d, J=7.8 Hz, 1H), 7.1

*た。抽出層を、水、炭酸水素ナトリウム水溶液及び飽和食塩水で順次洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの30:1の混合溶媒で流したところ、1-ジイソプロピルメチリデン-1,3-ジヒドロ-4-メトキシ-3,3-ジメチルイソベンゾフラン (化合物〔7〕) が544mg、収率61.0%で得られた。
 [0029] 融点: 48.0-48.5℃ (無色粒状晶、メタノールより再結晶)

¹H NMR (300MHz, CDCl₃); δ 1.09 (d, J=6.8 Hz, 6H), 1.25 (d, J=7.0 Hz, 6H), 1.56 (s, 6H), 2.43 (sept, J=7.0 Hz, 1H), 3.37 (sept, J=6.8 Hz, 1H), 3.84 (s, 3H), 6.69-6.77 (m, 1H), 7.18-7.26 (m, 2H) ppm
 IR (KBr); 2968, 2868, 1648, 1606, 1588 cm⁻¹
 Mass (m/z, %): 274 (M⁺, 68), 260 (44), 259 (100), 231 (58), 217 (13), 189 (17)
 [0030] (参考例5)
 [化13]

1 (t, J=7.8 Hz, 1H), 7.22 (d, J=7.8 Hz, 1H) ppm
 IR (KBr); 3516, 2976, 1646, 1616, 1588 cm⁻¹
 Mass (m/z, %): 260 (M⁺, 33), 245 (100), 217 (32)
 [0032] (参考例6)
 [化14]



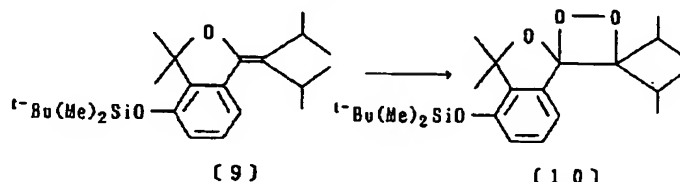
参考例5で合成した化合物〔8〕231mg (0.89 mmol) を無水DMF 3ml に溶解し、アルゴン雰囲気下0℃で攪拌した。この溶液にイミダゾール130mg (1.91 mmol) 及びt-ブチルジメチルクロシラン220mg (1.46 mmol) を加え室温で一晩攪拌した。反応混合物を水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥

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後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンで流しだしたところ、4'-t-ブチルジメチルシロキシ-1-ジイソプロピルメチリデン-1,3-ジヒドロ-3,3-ジメチルイソベンゾフラン(化合物〔9〕)が274mg、収率82.5%で得られた。

【0033】融点: 83.5-84.0°C(無色針状晶、メタノールと酢酸エチルより再結晶)

¹H NMR (300MHz, CDCl₃): δ 0.30 (s, 6H), 1.02 (s, 9H), 1.08 (d, J=6.8Hz, 6H), 1.25 (d, J=7.0Hz, 6H), 1.57 (s, 6H), 2.43 (sep, 6H), 1.57 (s, 6H), 2.43 (sep, 6H)



参考例6で合成した化合物〔9〕60mg (0.16mmol) 及びTPP 3mgをジクロロメタン20mlに溶解し、酸素雰囲気下-78°Cで攪拌した。この溶液にナトリウムランプ(180W)で2時間光照射を行った。反応混合物を濃縮し、濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの10:1の混合溶媒で流しだしたところ、4'-t-ブチルジメチルシロキシ-1',3'-ジヒドロ-4,4'-ジイソプロピル-3,3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-イソベンゾフラン](化合物〔10〕)が39mg、収率59.9%で無色不定形固体として得られた。

【0035】¹H NMR (300MHz, CDCl₃): δ 0.29 (s, 3H), 0.33 (s, 3H), 0.73 (d, J=7.4Hz, 3H), 0.98 (d, J=7.0Hz, 3H), 1.02 (s, 9H), 1.18 (d, J=7.1Hz, 3H), 1.35 (d, J=7.1Hz, 3H), 1.57 (s, 3H), 1.64 (s, 3H), 2.82-2.98 (m, 1H), 3.04-3.21 (m, 1H), 6.84 (d, J=8.0Hz, 1H), 7.26 (dd, J=8.0 and 7.8Hz, 1H), 7.56 (d, J=7.8Hz, 1H) ppm

IR (KBr): 2968, 2940, 1602, 1288 cm⁻¹

Mass (m/z, %): 374 (M⁺, 32.6), 359 (7), 292 (25), 236 (22), 235 (100)

【0036】(参考例7)

【化16】

12

* t, J=7.0Hz, 1H), 3.36 (sept, J=6.8Hz, 1H), 6.67 (d, J=7.9Hz, 1H), 7.11 (t, J=7.9Hz, 1H), 7.21 (d, J=7.9Hz, 1H) ppm

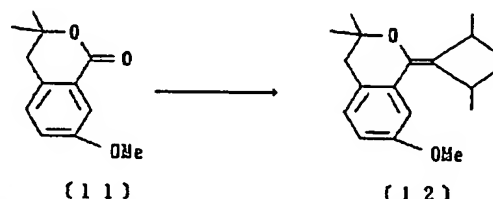
IR (KBr): 2956, 1646, 1588, 1274 cm⁻¹

Mass (m/z, %): 374 (M⁺, 32), 360 (29), 359 (100), 331 (20)

【0034】(実施例2)

【化15】

20



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酸素雰囲気下、0°Cで三塩化チタン4.5g (29.2mmol)を無水THF 75mlに懸濁した溶液に、水素化リチウムアルミニウム570mg (15.0mmol)を加え室温で攪拌した。この溶液にトリエチルアミン2.10ml (15.1mmol)を加え、15分間加熱還流した。この溶液に7-メトキシ-3,3-ジメチルイソクロマン-1-オン(化合物〔11〕)380mg (1.84mmol)及びジイソプロピルケトン1.8ml (12.7mmol)を無水THF 25mlに溶解して20分間かけて滴下し、さらに1時間加熱還流した。反応混合物を氷水に投じ酢酸エチルで抽出した。抽出層を、水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンとジクロロメタンの3:1の混合溶媒で流しだしたところ、1-ジイソプロピルメチリデン-7-メトキシ-3,3-ジメチルイソクロマン(化合物〔12〕)が215mg、収率40.5%で無色油状物として得られた。

40

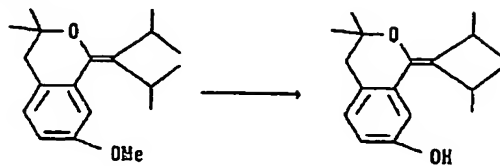
【0037】¹H NMR (400MHz, CDCl₃): δ 1.04 (d, J=6.8Hz, 6H), 1.15 (s, 6H), 1.28 (d, J=6.8Hz, 6H), 2.37 (sept, J=6.8Hz, 1H), 2.60 (s, 2H), 3.12 (sept, J=6.8Hz, 1H), 3.80 (s, 3H), 6.75 (dd, J=8.3 and 2.4Hz, 1H), 6.88 (d, J=2.4Hz, 1H), 7.00 (t, J=8.3Hz, 1H) ppm

Mass (m/z, %): 288 (M⁺, 6), 287

(21), 272 (39), 244 (29), 188 (43), 174 (16), 148 (100)

[0038] (参考例8)

[化17]



[12]

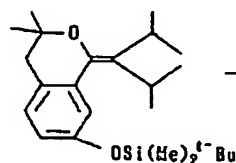
[13]

60%水酸化ナトリウム80mg (2.00mmol) を無水DMF 2mlに懸濁し、アルゴン雰囲気下0℃で攪拌した溶液に、エタンチオール0.15ml (2.03mmol) を加え、20分間攪拌した。この溶液に参考例7で合成した化合物[12] 175mg (0.608mmol) を無水DMF 1mlに溶解して加え、3時間加熱還流した。反応混合物を飽和食塩水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチル5:1の混合溶媒で流したところ、1-ジイソプロピルメチリデン-7-ヒドロキシ-3,3-ジメチルクロマン (化合物[13]) が159mg、収率95.5%で淡黄色油状物として得られた。

[0039] ^1H NMR (400MHz, CDCl₃) ; δ 1.03 (d, J=6.8Hz, 6H), 1.15 (s, 6H), 1.27 (d, J=6.8Hz, 6H), 2.36 (sept, J=6.8Hz, 1H), 2.58 (s, 2H), 3.09 (sept, J=6.8Hz, 1H), 4.93 (broad s, 1H), 6.68 (dd, J=8.3 and 2.4Hz, 1H), 6.80 (d, J=2.4Hz, 1H), 6.95 (d, J=8.3Hz, 1H) ppm
IR (liq. film) ; 3370, 2960, 1705, 1580 cm⁻¹

Mass (m/z, %) ; 274 (M⁺, 6), 273 (37), 258 (49), 230 (100), 174 (67), 160 (16), 146 (25)

[0040] (参考例9)

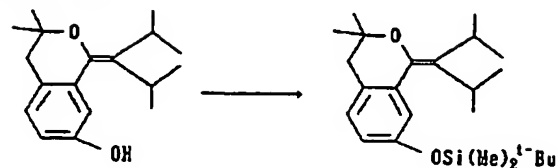


[14]

[15]

参考例9で合成した化合物[14] 85mg (0.219mmol) 及びTPP 5mgをジクロロメタン10mlに溶解し、酸素雰囲気下-78℃で攪拌した。この溶液にナトリウムランプ (940W) で2時間光照射を行った。反応混合物を濃縮し、濃縮物をシリカゲルカラム

* [化18]



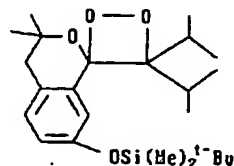
[13]

[14]

参考例8で合成した化合物[13] 121mg (0.442mmol) を無水DMF 5mlに溶解し、窒素雰囲気下0℃で攪拌した。この溶液にトリエチルアミン2.0ml (14.3mmol) 及びt-ブチルジメチルクロロシラン100mg (0.663mmol) を加え室温で2時間攪拌した。反応混合物を水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの10:1混合溶媒で流したところ、7-t-ブチルジメチルシロキシ-1-ジイソプロピルメチリデン-3,3-ジメチルイソクロマン (化合物[14]) が138mg、収率80.5%で無色油状物として得られた。

[0041] ^1H NMR (400MHz, CDCl₃) ; δ 0.19 (s, 6H), 0.99 (s, 9H), 1.03 (d, J=6.8Hz, 6H), 1.14 (s, 6H), 1.27 (d, J=6.8Hz, 6H), 2.35 (sept, J=6.8Hz, 1H), 2.58 (s, 2H), 3.09 (sept, J=6.8Hz, 1H), 6.70 (dd, J=7.8 and 2.4Hz, 1H), 6.81 (d, J=2.4Hz, 1H), 6.94 (d, J=7.8Hz, 1H) ppm
IR (liq. film) ; 2960, 2860, 1580, 1470, 1270 cm⁻¹
Mass (m/z, %) ; 388 (M⁺, 56), 373 (85), 345 (83), 288 (27), 234 (24), 220 (50), 206 (41), 73 (100)

[0042] (実施例3)
[化19]



にかけ、ヘキサンと酢酸エチルの10:1の混合溶媒で流したところ、7'-t-ブチルジメチルシロキシ-4,4-ジイソプロピル-3',3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-イソクロマン] (化合物[15]) が56mg、収率60.9%で淡黄

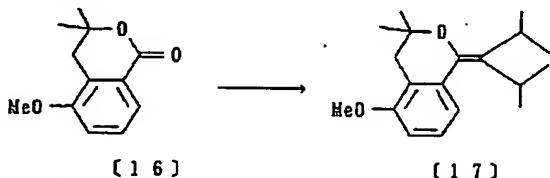
色油状物として得られた。

【0043】¹H NMR (400 MHz, CDCl₃) ; δ 0.23 (s, 6H), 0.46 (d, J = 7.3 Hz, 3H), 0.78 (d, J = 7.3 Hz, 3H), 0.91 (s, 3H), 1.00 (s, 9H), 1.16 (d, J = 7.3 Hz, 3H), 1.33 (d, J = 7.3 Hz, 3H), 1.48 (s, 3H), 2.61 (sept, J = 7.3 Hz, 1H), 2.63 (q, J = 5.0 Hz, 2H), 2.97 (sept, J = 7.3 Hz, 1H), 6.86 (d, J = 8.3 and 2.4 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H), 7.73 (d, J = 2.4 Hz, 1H) ppm

IR (liq. film) ; 2935, 1610, 1495, 1285 cm⁻¹

【0044】(参考例10)

【化20】



窒素雰囲気下、0℃で三塩化チタン4.5 g (29.2 mmol) を無水THF 75 ml に懸濁した溶液に、水素化リチウムアルミニウム570 mg (15.0 mmol) を加え、室温で攪拌した。この溶液にトリエチルアミン2.10 ml (15.1 mmol) を加え、15分間加熱還流した。この溶液に5-メトキシ-3,3-ジメチルイソクロマン-1-オン (化合物[16]) 61.8 mg (3.00 mmol) 及びジイソプロピルケトン1.8 ml (12.7 mmol) を無水THF 25 ml に溶解して20分間かけて滴下し、さらに1時間加熱還流した。反応混合物を氷水に投じ酢酸エチルで抽出した。抽出層を、水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンとジクロロメタンの3:1の混合溶媒で流したところ、1-ジイソプロピルメチリデン-5-メトキシ-3,3-ジメチルイソクロマン (化合物[17]) が620 mg、収率71.8%で無色油状物として得られた。

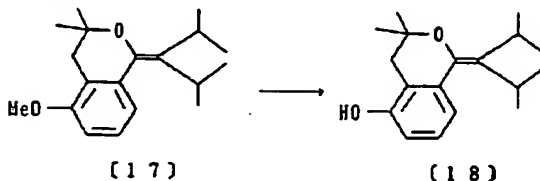
【0045】¹H NMR (400 MHz, CDCl₃) ; δ 1.02 (d, J = 6.8 Hz, 6H), 1.17 (s, 6H), 1.28 (d, J = 6.8 Hz, 6H), 2.36 (sept, J = 6.8 Hz, 1H), 2.69 (s, 2H), 3.07 (sept, J = 6.8 Hz, 1H), 3.83 (s, 3H), 6.7

8 (d, J = 7.8 Hz, 1H), 6.95 (d, J = 7.8 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H) ppm

IR (liq. film) ; 2985, 2870, 1580, 1475, 1365, 1265, 1130 cm⁻¹
Mass (m/z, %) ; 288 (M⁺, 18), 273 (41), 245 (37), 189 (39), 161 (25), 149 (100)

【0046】(参考例11)

10 【化21】



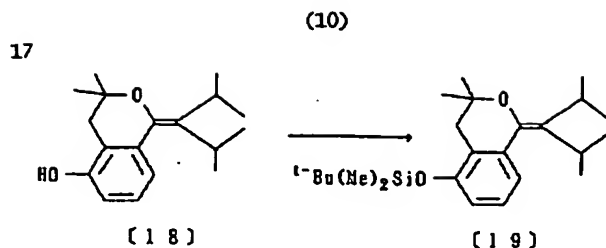
60%水素化ナトリウム80 mg (2.00 mmol) を無水DMF 2 ml に懸濁し、アルゴン雰囲気下0℃で攪拌した溶液に、エタノール0.15 ml (2.03 mmol) を加え、20分間攪拌した。この溶液に参考例10で合成した化合物[17] 215 mg (0.746 mmol) を無水DMF 1 ml に溶解して加え、3時間加熱還流した。反応混合物を飽和食塩水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチル5:1の混合溶媒で流したところ、1-ジイソプロピルメチリデン-5-ヒドロキシ-3,3-ジメチルイソクロマン (化合物[18]) が136 mg、収率66.5%で淡黄色油状物として得られた。

【0047】¹H NMR (300 MHz, CDCl₃) ; δ 1.02 (d, J = 6.8 Hz, 6H), 1.19 (s, 6H), 1.28 (d, J = 6.8 Hz, 6H), 2.36 (sept, J = 6.8 Hz, 1H), 2.67 (s, 2H), 3.07 (sept, J = 6.8 Hz, 1H), 4.68 (broad s, 1H), 6.69 (d, J = 7.8 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 7.06 (t, J = 7.8 Hz, 1H) ppm

IR (liq. film) ; 3400, 2960, 2870, 1655, 1580 cm⁻¹
Mass (m/z, %) ; 274 (M⁺, 52), 259 (54), 231 (78), 175 (100), 147 (21), 135 (46)

【0048】(参考例12)

【化22】



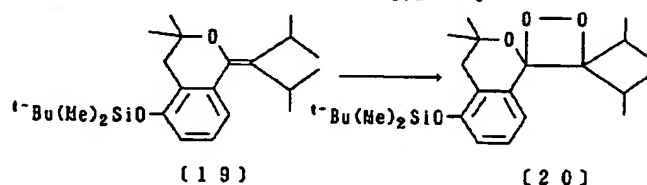
参考例11で合成された化合物〔18〕130mg (0.474mmol)を無水DMF 5mlに溶解し、窒素雰囲気下0℃で攪拌した。この溶液にトリエチルアミン2.0ml (14.3mmol)及びt-ブチルジメチルクロシラン100mg (0.663mmol)を加え室温で2時間攪拌した。反応混合物を水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの10:1混合溶媒で流しだしたところ、5'-t-ブチルジメチルシロキシー-1-ジイソプロピルメチリデン-3,3-ジメチルイソクロマン (化合物〔19〕)が142mg、収率77.1%で得られた。

【0049】融点: 88.0-89.0℃ (無色針状晶、ヘキサンと酢酸エチルで再結晶)

*¹HNMR (400MHz, CDCl₃): δ 0.21 (s, 6H), 1.01 (d, J=6.8Hz, 6H), 1.01 (s, 9H), 1.16 (s, 6H), 1.27 (d, J=6.8Hz, 6H), 2.36 (sept, J=6.8Hz, 1H), 2.66 (s, 2H), 3.07 (sept, J=6.8Hz, 1H), 6.72 (d, J=7.8Hz, 1H), 6.93 (d, J=7.8Hz, 1H), 7.04 (d, J=7.8Hz, 1H) ppm
IR (KBr): 2960, 2860, 1580, 1470, 1270 cm⁻¹
Mass (m/z, %): 388 (M⁺, 69), 373 (88), 345 (100), 289 (37)

【0050】(実施例4)

【化23】



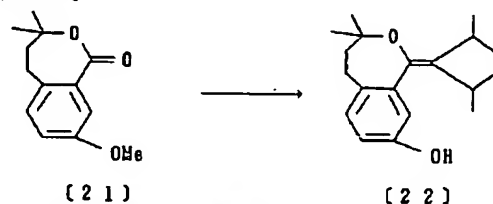
参考例12で合成した化合物〔19〕51mg (0.131mmol)及びTPP 5mgをジクロロメタン10mlに溶解し、窒素雰囲気下-78℃で攪拌した。この溶液にナトリウムランプ (940W) で2時間光照射を行った。反応混合物を濃縮し、濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの10:1の混合溶媒で流しだしたところ、5'-t-ブチルジメチルシロキシー-4,4-ジイソプロピル-3,3'-ジメチルスピロ [1,2-ジオキセタン-3,1'-イソクロマン] (化合物〔20〕)が30mg、収率54.3%で淡黄色油状物として得られた。

【0051】¹HNMR (400MHz, CDCl₃): δ 0.18 (s, 3H), 0.19 (s, 3H), 0.46 (d, J=7.3Hz, 3H), 0.74 (d, J=7.3Hz, 3H), 0.92 (s, 3H), 1.00 (s, 9H), 1.15 (d, J=7.3Hz, 3H), 1.33 (d, J=7.3Hz, 3H), 1.51 (s, 3H), 2.66 (q, J=15.3Hz, 2H), 2.54 (sept, J=7.3Hz, 1H), 2.98 (sept, J=7.3Hz, 1H), 6.89 (d with fine coupling, J=7.8Hz, 1H), 7.25 (t, J=7.8Hz, 1H), 7.90 (d, J=7.8Hz, 1H), 7.90 (d, J=7.8Hz, 1H)

z, 1H) ppm
IR (liq. film): 2930, 1470, 1255 cm⁻¹
Mass (m/z, %): 388 (M⁺ - 32, 7), 306 (38), 249 (35), 191 (100), 163 (17)

【0052】(参考例13)

【化24】



アルゴン雰囲気下、三塩化チタン5.0g (32.4mmol)を無水THF 100mlに懸濁して15分間攪拌した後、氷冷して水素化リチウムアルミニウム629mg (16.6mmol)を加え、室温で30分間攪拌した。この溶液にトリエチルアミン2.30ml (16.5mmol)を加え、30分間加熱還流した。この溶液に8-メトキシ-3,3-ジメチル-2-ベンゾオキセパン-1-オン (化合物〔21〕) 695mg (3.16mmol)及びジイソプロピルケトン0.9

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5 ml (6.71 mmol) を無水THF 20 ml に溶解して30分間かけて滴下し、さらに1時間加熱還流した。反応混合物を氷水に投じ酢酸エチルで抽出した。抽出層を水、炭酸水素ナトリウム水溶液及び飽和食塩水で順次洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチルの20:1の混合溶媒で流しだしたところ、1-ジイソプロピルメチリデン-8-メトキシ-3,3-ジメチル-2-ベンゾオキセパン (化合物〔22〕) が128 mg、収率13.4%で得られた。

【0053】融点: 55.0-56.0°C (無色針状晶、メタノールより再結晶)

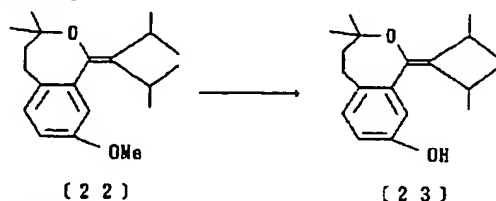
¹H NMR (300 MHz, CDCl₃): δ 0.96 (d, J=6.8 Hz, 6H), 1.07 (broad s, 6H), 1.26 (d, J=7.0 Hz, 6H), 1.76-1.94 (m, 2H), 2.59 (sept, J=7.0 Hz, 1H), 2.67 (sept, J=6.8 Hz, 1H), 2.27-2.86 (m, 2H), 3.78 (s, 3H), 6.71-6.78 (m, 2H), 7.00 (d, J=9.2 Hz, 1H) ppm

IR (KBr): 2968, 2928, 2864, 1616, 1574 cm⁻¹

Mass (m/z, %): 302 (M⁺, 61), 259 (100), 231 (14), 204 (28), 203 (89), 189 (37), 175 (34), 161 (20)

【0054】(参考例14)

【化25】



60%水素化ナトリウム30 mg (0.750 mmol) 及び参考例13で合成した化合物〔22〕89 mg (0.295 mmol) を無水DMF 1.75 ml に懸濁し、アルゴン雰囲気下0°Cで攪拌した溶液に、エタノール0.06 ml (0.810 mmol) を加え、室温で15分間攪拌した。この溶液を130°Cで3時間、続いて150°Cで1時間30分間加熱攪拌した。反応混合物を飽和食塩水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンと酢酸エチル10:1の混合溶媒で流しだしたところ、1-ジイソプロピルメチリデン-8-ヒドロキシ-3,3-ジメチル-2-ベンゾオキセパン (化合物〔23〕) が45 mg、収率53.0%で無色不定形固体として得られた。

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【0055】¹H NMR (300 MHz, CDCl₃):

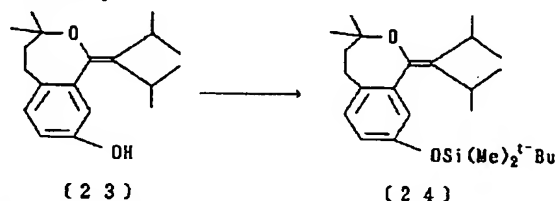
δ 0.95 (d, J=6.9 Hz, 6H), 1.07 (broad s, 6H), 1.25 (d, J=7.1 Hz, 6H), 1.78-1.90 (m, 2H), 2.58 (sept, J=7.1 Hz, 1H), 2.66 (sept, J=6.9 Hz, 1H), 2.70-2.84 (m, 2H), 4.54 (s, 1H), 6.63-6.70 (m, 2H), 6.96 (d, J=7.8 Hz, 1H) ppm

IR (KBr): 3400, 2960, 2932, 2872, 1712, 1608, 1580 cm⁻¹

Mass (m/z, %): 288 (M⁺, 66), 245 (100), 217 (14), 189 (85), 175 (28), 161 (32), 147 (18)

【0056】(参考例15)

【化26】



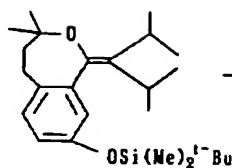
参考例14で合成された化合物〔23〕43 mg (0.15 mmol) を無水DMF 1.5 ml に溶解し、アルゴン雰囲気下室温で攪拌した。この溶液にイミダゾール28 mg (0.41 mmol) 及びt-ブチルジメチルクロロシラン51 mg (0.34 mmol) を加え室温で一晩攪拌した。反応混合物を水に投じ酢酸エチルで抽出した。抽出層を飽和食塩水で洗浄、硫酸マグネシウム乾燥後濃縮した。濃縮物をシリカゲルカラムにかけ、ヘキサンとエーテルの20:1混合溶媒で流しだしたところ、8-t-ブチルジメチルシロキシ-1-ジイソプロピルメチリデン-3,3-ジメチル-2-ベンゾオキセパン (化合物〔24〕) が52 mg、収率82.6%で無色油状物として得られた。

【0057】¹H NMR (300 MHz, CDCl₃): δ 0.16 (s, 6H), 0.94 (d, J=6.9 Hz, 6H), 0.97 (s, 9H), 0.86-1.10 (m, 6H), 1.26 (d, J=7.0 Hz, 6H), 1.78-1.90 (m, 2H), 2.50 (sept, J=7.0 Hz, 1H), 2.68 (sept, J=6.9 Hz, 1H), 2.68-2.84 (m, 2H), 6.66-6.72 (m, 2H), 6.95 (d, J=8.6 Hz, 1H) ppm

IR (liq. film): 2960, 2932, 2864, 1606, 1572, 1288 cm⁻¹

Mass (m/z, %): 403 (M⁺+1, 25), 402 (M⁺, 76), 360 (29), 359 (100), 304 (32), 303 (80), 289 (3

【0058】(実施例5)



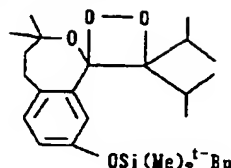
(24)

参考例15で合成した化合物〔24〕48mg (0.12mmol) 及びTPP4mgをジクロロメタン20mlに溶解し、酸雰囲気下-78℃で攪拌した。この溶液にナトリウムランプ(180W)で3時間光照射を行った。反応混合物を濃縮し、濃縮物をシリカゲルカラムにかけ、ヘキサンとエーテルの20:1の混合溶媒で流しだしたところ、8'-t-ブチルジメチルシロキシ-4,4'-ジイソプロピル-3',3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-(2'-ベンゾオキセパン)](化合物〔25〕)が45mg、収率8.8%で無色不定形固体として得られた。

【0059】¹H NMR (300MHz, CDC1₃) ; δ 0.21 (s, 6H), 0.53 (d, J=7.1Hz, 3H), 0.75 (d, J=7.0Hz, 3H), 0.85 (s, 3H), 0.99 (s, 9H), 1.25 (d, J=7.1Hz, 3H), 1.38 (s, 3H), 1.45 (d, J=7.0Hz, 3H), 1.65 (td, J=13.1 and 4.4Hz, 1H), 2.00 (ddd, J=13.1, 5.3 and 2.6Hz, 1H), 2.32 (sept, J=7.1Hz, 1H), 2.41 (ddd, J=13.4, 4.4 and 2.6Hz, 1H), 2.77 (sept, J=7.0Hz, 1H), 3.09 (td, J=13.4 and 5.3Hz, 1H), 6.80 (dd, J=8.1 and 2.6Hz, 1H), 6.93 (d, J=8.1Hz, 1H), 7.59 (d, J=2.6Hz, 1H) ppm

IR (KBr) : 2968, 2936, 1608, 1274 cm⁻¹

* * 【化27】



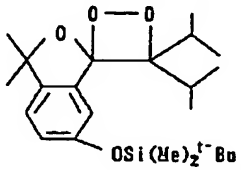
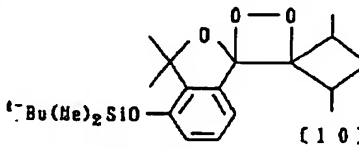
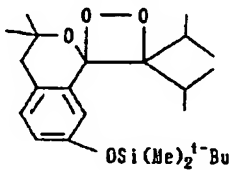
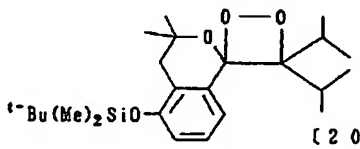
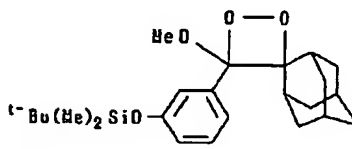
(25)

Mass (m/z, %): 434 (M⁺, 0.1), 402 (38), 359 (17), 320 (42), 263 (24), 207 (100), 205 (19)

【0060】(試験例1) 実施例1、2、3及び4において得られた6'-t-ブチルジメチルシロキシ-1',3'-ジヒドロ-4,4'-ジイソプロピル-3',3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-イソベンゾフラン](化合物〔5〕)、4'-t-ブチルジメチルシロキシ-1',3'-ジヒドロ-4,4'-ジイソプロピル-3',3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-イソベンゾフラン](化合物〔10〕)、7'-t-ブチルジメチルシロキシ-4,4'-ジイソプロピル-3',3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-イソクロマン](化合物〔15〕)及び5'-t-ブチルジメチルシロキシ-4,4'-ジイソプロピル-3',3'-ジメチルスピロ[1,2-ジオキセタン-3,1'-イソクロマン](化合物〔20〕)の1.8×10⁻⁴M DMSO溶液1mlを、それぞれテトラブチルアンモニウムフルオリドの1.0×10⁻³M DMSO溶液2mlに25℃に加え、そのときの発光を蛍光分析計で測定した。このときの発光の量子収率及び半減期を表に示した。なお、比較として4-(3-t-ブチルジメチルシリルオキシフェニル)-4-メトキシスピロ[1,2-ジオキセタン-3,2'-アダマンタン]も同様の測定条件で測定し、発光の半減期を表に示した。

【0061】

【表1】

化 合 物	化学発光 量子収率	λ_{max}	化学発光 の半減期 (秒)
 (5)	0.15	456	153
 (1 0)	>0.12	438	3329
 (1 5)	>0.10	486	4520
 (2 0)	0.28	472	23.5
 (2 5)	(0.25)	463 (470)	4.7 (5.0)

()内はA. P. Schaap, et al., Tetrahedron Lett., 28, 1155(1987)参照

[0062]

【発明の効果】本発明の1, 2-ジオキセタン誘導体
(I)は、発光持続性が著しく長いという特徴を有して*

*いる。即ち、発光開始後は安定した発光が持続するた
め、安定した測定データが得られ再現性の高い結果とな
る。

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